The Medical Journal of Australia – Preprint only – 3 April 2020

Cardiovascular Disease and COVID-19: Australian/New Zealand Consensus Statement

Sarah Zaman
Academic Interventional Cardiologist
Monash University Faculty of Medicine Nursing and Health Sciences
MonashHeart, Monash Medical Centre
Melbourne, Victoria
Australia

Andrew I MacIsaac
Cardiologist
St Vincent's Hospital, Melbourne
Department of Cardiology
Fitzroy, Victoria
Australia

Garry LR Jennings
Executive Director
Sydney Health Partners
University of Sydney
Sydney Medical School
University of Sydney
Sydney, New South Wales
Australia

Senior Director
Baker Heart & Diabetes Institute
Alfred Centre
Melbourne, Victoria
Australia

Markus Schlaich
University of Western Australia
Faculty of Medicine Dentistry and Health Sciences
Dobney Hypertension Centre
Perth Western Australia
Australia

Sally C Inglis
Senior Research Fellow
University of Technology, Sydney
Faculty of Health
Sydney, New South Wales
Australia

Ruth Arnold
Cardiologist
Orange Health Service
Department of Cardiology
Orange, New South Wales
Australia

Derek P Chew
Professor of Cardiology
Flinders University
Department of Cardiology
Adelaide, South Australia
Australia

Saurabh Kumar
Cardiologist and Electrophysiologist
Westmead Hospital
Department of Cardiology
Westmead, New South Wales
Australia

The University of Sydney
Westmead Applied Research Centre
Westmead, New South Wales
Australia

Liza Thomas
Westmead Hospital
Department of Cardiology
Westmead, New South Wales
Australia

University of Sydney
Department of Medicine
Sydney, New South Wales

Australia

Sudhir Wahi
Director of Echocardiography and Senior Staff Cardiologist
Brisbane Heart
Department of Cardiology
Woolloongabba, Queensland
Australia

Stephan J Duffy
Head of Cardiology General Services
Alfred Hospital
Department of Cardioolgy
Melbourne, Victoria
Australia

Sidney Lo
Liverpool Hospital
Department of Cardiology
Liverpool, New South Wales
Australia

Andrew Newcomb
Cardiac Surgeon
St Vincent's Clinical School
Department of Cardiothoracic Surgery
Melbourne, Victoria
Australia

Aubrey Almeida
Epworth Richmond Hospital
Cardiac Sciences Clinical Institute
Melbourne, Victoria
Australia

Monash Health
Department of Cardiothoracic Surgery
Melbourne, Victoria
Australia

Carolyn Naismith
Austin Hospital
Department of Cardiology
Melbourne, Victoria
Australia

Mayanna Lund
Doctor
Middlemore Hospital
Department of Cardiology
Middlemore Hospital
Auckland, New Zealand

Stephen Nicholls
Cardiologist
Monash Health
MonashHeart
Melbourne, Victoria
Australia

Selwyn Wong
Middlemore Hospital
Department of Cardiology
Auckland, New Zealand

Leonard Kritharides
Professor
Concord Hospital
Department of Cardiology
Sydney, New South Wales
Australia

Group Leader/Deputy Director
ANZAC Research Institute
Atherosclerosis Laboratory
Sydney, New South Wales
Australia

Clara K Chow
Professor of Medicine
University of Sydney

Westmead Clinical School
Westmead Hospital
Westmead, New South Wales
Australia

Program Director
Community Based Cardiac Services
Westmead Hospital
Department of Cardiology
Westmead, New South Wales
Australia

Ravi Bhindi
Royal North Shore Hospital
Department of Cardiology
St Leonards, New South Wales
Australia

The Medical Journal of Australia – Preprint only – 3 April 2020

Endorsed by:

Cardiac Society of Australian and New Zealand (CSANZ)

National Heart Foundation (NHF)

High Blood Pressure Research Council of Australia (HBPRCA)

Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS)

Word Count: 2,388 (main body text)

Word count: 244 (abstract)

ABSTRACT

The Medical Journal of Australia – Preprint only – 3 April 2020

Introduction: The Coronavirus-19 disease (COVID-19) pandemic is caused by 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 healthcare 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 (CSANZ) Board and Council members, Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS), 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. Patients with pre-existing CVD are more susceptible to life threatening SARS-CoV-2 infection. Special precautions are needed to avoid viral transmission to this at-risk population. Innovative health care delivery models and resource allocation are required throughout the health care system to address this need.

Changes in management: Cardiovascular health services and cardiovascular healthcare 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 CSANZ, ANZSCTS, National Heart Foundation (NHF), and the High Blood Pressure Research Council of Australia (HBPRCA) summarises important issues and proposes practical approaches to cardiovascular healthcare delivery to patients with and without SARS-CoV-2 infection.

INTRODUCTION

On March 11th, 2020 the World Health Organisation declared coronavirus disease 2019 (COVID-19) a pandemic. The presence of underlying cardiovascular disease (CVD) confers the highest mortality with COVID-19 disease, thus patients with CVD must be considered a particularly at-risk population(1-5). Community transmission, patient-to-patient transmission and healthcare worker infection with SARS-CoV-2 are overwhelming health services worldwide (4,6). High-quality cardiac care must minimise risk of viral transmission to patients and healthcare workers. It should adapt resources in the context of reduced access to hospital beds and personal protective equipment (PPE). This paper reviews and summarises data on SARS-CoV-2 infection in pre-existing CVD, acute cardiovascular manifestations of COVID-19 and; makes recommendations for cardiac service provision during this pandemic.

Development Process for the Following Recommendation (METHODS)

A group of CVD experts was drawn from the Cardiac Society of Australia/New Zealand (CSANZ), Australian/NZ Society of Cardiac and Thoracic Surgeons (ANZSCTS), National Heart Foundation (NHF) and the High Blood Pressure Research Council of Australia (HBPRCA) were convened in March 2020. Key opinion leaders from cardiology, cardiothoracic surgery and public health with broad geographic representation were consulted. Major databases were searched to identify relevant systematic reviews, randomised controlled trials (RCT) and clinical case series in English from inception to 25th March 2020. As there were no completed prospective cohort studies nor RCTs relating to COVID-19 and CVD, 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 and prevention and rural) generated key recommendations from their respective council and/or craft group. In addition, social networking platforms (WhatsApp) involving CSANZ board members, cardiology heads of department and key opinion leaders was 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 prior to 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 8 studies and >46,000 patients in China reported 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 (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 (CFR) rates; 5-fold higher than the overall COVID-19 infected population (**Table 1**)(4). In Italy the overall CFR (7.2%) was higher than that in China, with a high prevalence of baseline CVD in fatal cases(11). *Patients with CVD are at heightened risk of COVID-19 and health services and patients should take additional pre-cautions.*

Angiotensin-converting enzyme-inhibitors and angiotensin receptor blockers

As the SARS-CoV-2 virus enters cells via 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 of these patients(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), and in some animal models treatment with ACE-I or ARBs can increase the expression and activity of ACE-2(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 ACE-2 and the ARB losartan are currently being tested in the US as potential COVID-19 therapies(17). *Given the well-established beneficial effects of ACEI/ARB in patients with hypertension, heart failure and CVD, it is the strong recommendation of the authors and numerous national and international societies that these medications should be continued as indicated*(18-20).

Acute cardiac injury and COVID-19

Acute cardiac injury in COVID-19 manifests as left ventricular (LV) dysfunction, heart failure, ventricular arrhythmias, ECG changes, elevated B-type natriuretic peptide (BNP) and troponin(2,21-23). 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%(2). A later study found acute cardiac injury in 19.7%(22) while a US study of 21 intensive care patients described cardiomyopathy in 33%(21). Acute cardiac injury was independently associated with mortality in hospitalised COVID-19 patients in China(22).

Pathophysiological theories for cardiac injury include direct infection of the myocardium with SARS-Co-2, myocardial inflammation, Takotsubo syndrome or overwhelming multi-organ illness. 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(24). Myocardial inflammatory infiltrates were instead seen(24). For patients with LV dysfunction, ACE-I/ARB's and beta-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 and myocardial infarction

Troponin and other cardiac enzymes are commonly elevated in COVID-19(2,3,5,21,25). Troponin elevation is a prognostic marker and may reflect myocarditis or myocardial infarction (MI)(26). The diagnostic implications are unclear as it can be associated with non-coronary conditions including acute respiratory infections(27), and Type 2 MI (28). Myocardial injury in COVID-19 patients can manifest with ST-elevation in the absence of obstructive coronary artery disease (CAD). Whether this is due to microvascular injury or myocarditis is unclear. *To avoid unnecessary coronary angiography during the acute illness, haemodynamically stable patients with COVID-19 and possible MI may be best managed conservatively, with invasive procedures deferred until after COVID-19 recovery.*

Cardiovascular implications of novel therapies

Numerous clinical trials assessing treatment for COVID-19 are being conducted. Chloroquine, hydroxychloroquine, azithromycin and ritonavir/lopinavir amongst others, 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(29). *Off-label prescribing of hydroxychloroquine has been reported(30) and health professionals should be alert to cardiac toxicity in the community.*

RECOMMENDATIONS FOR CARDIOVASCULAR HEALTHCARE 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 1**). All health services need to review elective procedures in order to increase hospital capacity and conserve valuable personal protection equipment (PPE). Alternative healthcare for patients at risk for COVID-19 that avoids exposure within the hospital system requires multi-disciplinary assessment. As COVID-19 cases could exceed respiratory and intensive care bed capacity, coronary care unit beds may be re-allocated and cardiac critical care nurses redeployed. Cardiac procedures that require long-length or ICU stay, should be carefully considered due to their impact on bed availability. A high 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. Highly symptomatic or unstable patients should be prioritised. Rapid discharge strategies should be instituted, including same-day discharge for elective percutaneous coronary intervention (PCI), and next-day discharge for stable non-ST elevation MI (NSTEMI) following revascularization. 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 (CCL). Bringing a COVID-19 positive patient (known or unknown) to the CCL exposes staff to the risk of infection, and prevents CCL use post-procedure pending a terminal clean. Delays are to be expected with primary PCI (PPCI) to allow for COVID-19 assessment and infection control measures. STEMI protocols during the COVID-19 pandemic have been published from China, Spain and the US(23,28,31). The Sichuan Provincial People's Hospital proposed fibrinolytic therapy for all STEMI's with suspension of their PPCI service(28). This lysis protocol relied on rapid nucleic acid testing, not yet available in Australia (but likely to be soon). The US and Spanish Cardiology Society recommended PPCI continuation with appropriate PPE, and lysis for select cases(23,31). In Australia, each healthcare service will be different, but it is important that a local protocol is developed and adapted, with CSANZ guidance available (**Figure 2**)(32). Training in PPE, sourcing fibrinolytic medications and updating lysis protocols are critical. As COVID-19 is associated with STEMI 'mimickers' (ST elevation without obstructive CAD due to microvascular thrombosis or myocarditis), use of lysis may confer risk without benefit in some cases, exacerbated by COVID-associated coagulation abnormalities (17,23). Bedside echocardiogram to ascertain regional wall abnormalities and CT coronary angiography to limit CCL staff exposure could all be considered.

Coronary angiography criteria in NSTEMI patients' needs reconsideration. Reliance on the presence of an elevated troponin level to indicate ACS in COVID-19 patients will be misleading. Greater emphasis should be given to high-risk clinical features (recurrent chest pain, dynamic ischaemic ECG changes, heart failure, haemodynamic instability, and major

arrhythmias) and the presence of regional wall motion abnormalities on echocardiography. It is reasonable to defer invasive investigations in stable patients without high risk features, especially when the patient is COVID-19 positive.

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 to regional and rural centres, will be needed. Centralised ECG-reading services are well placed to co-ordinate transfer logistics with linked calls between cardiologists, 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, whilst balancing the enormous resourcing demands that COVID-19 will place on healthcare systems.

Cardiothoracic Surgery Considerations

The Australian government has currently stopped non-urgent surgery. Patients will likely continue to present with symptomatic coronary disease and be referred for cardiac surgery, and up to half of these patients will not be well enough to discharge pre-surgery. Cardiac surgical cases are likely to take longer during the pandemic due to infection control measures, and access to ICU will be limited. COVID-free patients recovering from cardiac surgery in ICU require separation from suspected or proven COVID-19 ICU patients. Many

patients undergoing cardiac surgery are frail or have significant comorbidities, hence the risk of ICU management may outweigh the benefits of operative treatment, with multidisciplinary consideration required. Establishing or re-establishing Cardiac Surgical ICU programs could be possible and free-up precious general ICU resources. Cardiac surgical ICU management is widespread in the USA and outcomes are equivalent to general ICU(33). It will be imperative for the heart team to consider and adjust the threshold for management of severe CAD with coronary artery bypass graft surgery, PCI or medical therapy. The same applies to surgical aortic valve replacement or transcatheter aortic valve implantation for patients with 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 on ventilator use, bed stay and recovery time.

Key considerations in management of 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 transesophageal echo (TOE) pose significant viral transmission risk. TOE involves instrumentation of the oro-pharynx, known to harbour the virus with high risk of aerosol/ airborne transmission(34) and should be undertaken only if other investigations have been exhausted (i.e. serial TTEs in suspected endocarditis) or after exclusion of COVID-19. If TOE is performed, it should be performed in a negative pressure room or with patient intubation, with appropriate PPE. In admitted COVID-19 patients, non-invasive ventilation such as continuous (CPAP)/bilevel positive

airway pressure (BiPAP) and high flow oxygen are aerosol generating and not recommended(34,35).

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, electrophysiologic (EP) interventions, implantation and follow-up of cardiac implanted electronic devices (CIED) (**Box 4**). 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 care - identifying suitable patients for 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 with screening of all patients for suitability(36). For in-person consultations a single point of clinic entry with verbal/temperature screening and 1.5 metres between seated patients is recommended, with steps to reduce patient numbers in waiting rooms by staggering appointment times and having patients wait in their cars. Administrative teams should be supported in their ability to maintain physical distancing to reduce their own exposure.

Nurse-led clinics, cardiac rehabilitation programs and **patient self-management** will need to adapt through utilisation of tele-health 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 enable titration of medications. Online support can enable patients to continue cardiac rehabilitation during home isolation (**Box 5**). CVD professionals are well positioned to provide patient education about COVID-19. Patients should be encouraged to notify their treating doctor regarding clinical status deterioration and to call 000 (111 in New Zealand) in an emergency, despite healthcare system overload. It will be important for cardiovascular patients to have conversations with their clinicians and family regarding advanced care planning.

Healthcare workers

There is a considerable risk of SARS-CoV-2 infection for healthcare workers (HCWs)(4,6). Healthcare 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 correct PPE donning/doffing training. Services will need to adapt to HCW shortage and extended leave due to illness or quarantine. Cardiology trainees will be at the forefront of service change implementation and 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. Links to relevant documents and important websites can be found in **Box 5**, including the Australian Health Practitioner Regulation Agency statement on medicolegal considerations during COVID-19(37).

Conclusions

COVID-19 will have a significant and lasting impact on the practice of Cardiology in Australia and New Zealand. The preparation and adaptability of the cardiac team will be critical to respond to this global COVID-19 crisis.

REFERENCES

1. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-513.

2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

3. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020.

4. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020.

5. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis. 2020.

6. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. JAMA. 2020.

7. European Society of Cardiology (ESC). https://www.escardio.org/Education/COVID-19-and-Cardiology. Last accessed 25th March 2020.

8. American College of Cardiology (ACC). https://www.acc.org/latest-in-cardiology/features/accs-coronavirus-disease-2019-covid-19-hub#sort=%40fcommonsortdate90022%20descending. Last accessed 25th March 2020. .

9. British Cardiovascular Society (BCS). https://www.britishcardiovascularsociety.org/resources/covid-19-clinicians-hub. Last accessed 25th March 2020.

10. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). Eur J Intern Med. 2020.

11. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020.

12. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020.

13. Tikellis C, Thomas MC. Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease. Int J Pept;2012:256294.

14. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med. 2020.

15. Ferrario CM, Jessup J, Chappell MC, et al. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation. 2005;111(20):2605-2610.

16. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med. 2005;11(8):875-879.

17. Zhang H, Penninger JM, Li Y, et al. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 2020.

18. High Blood Pressure Research Council of Australia. https://www.hbprca.com.au/wp-content/uploads/2020/03/HBPRCA-Statement-on-COVID-19-and-BP-medication-17.03.20.pdf. Accessed 25th March 2020.

19. De Simone G, Chair ESC Council on Hypertension. https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-

statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang. Last accessed March 25th 2020.

20. International Society of Hypertension. https://ish-world.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19/. Last accessed 25th March 2020.

21. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020.

22. Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020.

23. Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the Coronavirus Disease 2019 (COVID-19) Pandemic. J Am Coll Cardiol. 2020.

24. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020.

25. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020.

26. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis. 2020.

27. Rivara MB, Bajwa EK, Januzzi JL, et al. Prognostic significance of elevated cardiac troponin-T levels in acute respiratory distress syndrome patients. PLoS One. 2012;7(7):e40515.

28. Zeng J, Huang J, Pan L. How to balance acute myocardial infarction and COVID-19: the protocols from Sichuan Provincial People's Hospital. Intensive Care Med. 2020.

29. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020:105949.

30. Therapeutic Goods Administration. https://www.tga.gov.au/alert/new-restrictions-prescribing-hydroxychloroquine-covid-19. Accessed 25th March 2020.

31. Rafael-Romaguera IC-Gl, Soledad Ojeda et al. https://www.recintervcardiol.org/images/pdf-files/RECIC_20_E201_Romaguera_COVID_AE_UKtrad_0324.pdf. REC Interv Cardiol (article in press). Accessed 25th March 2020.

32. Cardiac Society of Australia and New Zealand (CSANZ). https://www.csanz.edu.au/covid-19/. Accessed 25th March 2020.

33. Lee LS, Clark AJ, Namburi N, et al. The presence of a dedicated cardiac surgical intensive care service impacts clinical outcomes in adult cardiac surgery patients. J Card Surg. 2020.

34. Brewster DJ CN, DO T, et al. Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group. Medical Journal of Australia. 2020;epub.

35. Cheung JC, Ho LT, Cheng JV, et al. Staff safety during emergency airway management for COVID-19 in Hong Kong. Lancet Respir Med. 2020; epub.

36. Medicare Benefits Schedule. http://www.mbsonline.gov.au. Telehealth item numbers. Accessed 25th March 2020.

37. Australian Health Practitioner Regulation Agency. https://www.ahpra.gov.au/News/2020-03-12-Statement-from-the-National-Boards-and-Ahpra-COVID-19.aspx. Medicolegal considerations of COVID-19. Accessed 25th March 2020.

38. Australian Government Department of Health. https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers. Accessed 25th March 2020.

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

Condition*	**Case fatality rates (CFR)**
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 CFR of 2.3% (1,023 deaths)(4).

Box 1. Assessment of patient's risk for COVID-19

- Clinical and radiological risk factors
    - Fever>37.5 (patients may have no or low-grade fever on presentation)
    - Cough, shortness of breath or sore throat
    - Any flu-like symptoms in a healthcare worker
    - Contact with a confirmed COVID-19 contact in the last 14 days
    - Arrival from overseas in the last 14 days
    - Lymphocyte count <1.5
    - Bi-basal ground glass appearance (CT) or bi-basal pneumonia (CXR)

Of note these risk factors may change, updated information on Department of Health(38)

Box 2. General considerations for cath lab use during COVID-19 pandemic

- Determine patient's COVID-19 status (as per **Box 1)**
    - When available consider rapid point of care testing, if unable to obtain history (e.g. intubated patient) consider the patient to be at-risk
- For all confirmed/suspected COVID-19 cases:
    - Patient - surgical/medical mask if not intubated
    - PPE for all cath lab staff including aerosol protection (N95 mask) given risk of emergent intubation/CPR/vomiting in STEMI (aerosol generating procedures)
- Patients approaching/requiring intubation should have this performed prior to transfer to CCL as intubation/suction/active CPR all increase aerosolization of respiratory secretions
- Designated 'dirty' COVID-19 cath labs within each institution that are cleared of non-essential equipment/stock to facilitate cleaning. Consider dedicated, in the lab, stock for COVID-19 patients
- Number of staff required to be in the cath lab should be limited to essential personnel only e.g.: Cardiologist, scrub assistant, scout nurse
- Minimise or abolish staff movements in and out of the lab during the case
- Instituting a dedicated nurse role outside the lab to allow for passing equipment and medication, coordination of destination teams for transfer, facilitating correct use of PPE and ensure adherence to infection control protocols
- A terminal clean following the procedure will be required, with potential for delays in subsequent cases

Box 3. General considerations for TTE/TOE during COVID-19

- PPE for healthcare provider/assistants performing the test
- Shorten study duration to reduce face-to-face contact e.g. limiting TTE to 15 minutes
- Dedicated 'COVID-19' machine/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/ portable echo's if available
- TOE 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-ECG and exercise stress echo have high respiratory transmission risk and careful consideration should be given to if these services should be suspended
- In admitted patients, non-invasive ventilation such as continuous (CPAP)/bilevel positive airway pressure (BiPAP) and high flow oxygen are aerosol generating and not recommended

Box 4. General considerations for electrophysiology/pacing during COVID-19

For cardiac implanted electronic devices (CIED) follow up:

- Avoid in person clinics, hospitals and office visits
- Use remote monitoring/telehealth
- For major problems (e.g. lead/battery or device therapies in defibrillator patients), perform risk/benefit of delayed visit versus risk of COVID-19 exposure

Requests for urgent CIED interrogation by wards and emergency departments

- Use remote monitoring and/or manual transmissions
- Face to face interrogation requires PPE and minimise number of technicians with wireless technology if possible

Defer elective electrophysiology procedures for 1- 3 months until PPE stocks sufficient

- Urgent procedures to be continued: pacemaker for AV 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 ECG monitors.

Box 5. Important online resources for cardiology teams during COVID-19

- CSANZ sharing portal: https://www.csanz.edu.au/covid-19/
- ACC COVID-19 hub: https://www.acc.org/covid19#sort=%40fcommonsortdate90022%20descending
- European Society of Cardiology: COVID-19 and Cardiology: https://www.escardio.org/Education/COVID-19-and-Cardiology
- British Cardiovascular Society- COVID-19 Clinician's Resource Hub: https://www.britishcardiovascularsociety.org/resources/covid-19-clinicians-hub
- Australian College of Nursing COVID-19 resources: https://www.acn.edu.au/covid-19-resources
- Palliative Care Australia –Advanced Care Planning: https://palliativecare.org.au/covid-19-updates
- Exercise advice and videos to support people with cardiovascular disease to keep exercising during isolation: https://baker.edu.au/health-hub/keep-it-moving; https://www.healtheuniversity.ca/en/cardiaccollege
- Telehealth item numbers available at: http://www.mbsonline.gov.au
- Australian Health Practitioner Regular Agency (AHPRA): https://www.ahpra.gov.au
- Department of Health: https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbersTelehealth item numbers available at: http://www.mbsonline.gov.au

Figure 1. Acute cardiovascular manifestations of COVID-19

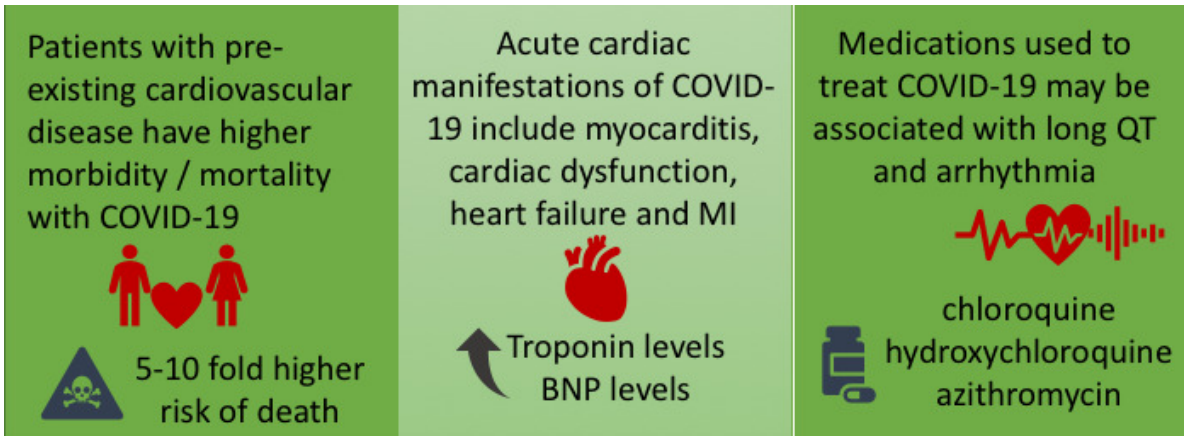

Figure 2. General principles to consider for management of STEMI during COVID-19 Pandemic

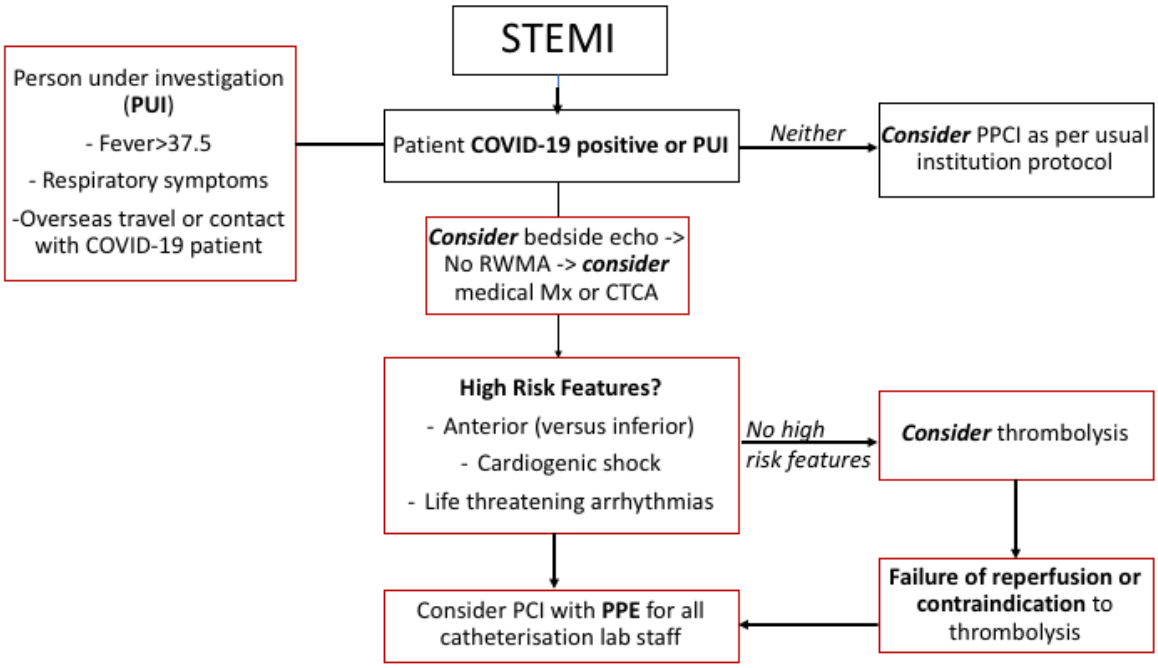

Figure legend: At any stage in this pathway either PPCI or thrombolysis could be considered. The availability of rapid COVID-19 testing, when available, may alter this protocol.

STEMI=ST elevation myocardial infarction; PPCI=primary PCI; RWMA= regional wall motion abnormality. PPE= personal protection equipment.