Multimodality Imaging in Evaluation of Cardiovascular complications in Patients with COVID-19

Lawrence Rudski, MD, James L. Januzzi, MD, Vera H. Rigolin, MD, Erin A. Bohula, MD, DPhil, Ron Blankstein, MD, Amit R. Patel, MD, Chiara Bucciarelli-Ducci, MD, PhD, FESC, FRCP, Esther Vorovich, MD, MSCE, Monica Mukherjee, MD, MPH, Sunil V. Rao, MD, FSCAI, Rob Beanlands, MD, Todd C. Villines, MD, Marcelo F. Di Carli, MD

PII: S0735-1097(20)36039-3

DOI: https://doi.org/10.1016/j.jacc.2020.06.080

Reference: JAC 27553

To appear in: *Journal of the American College of Cardiology*

Received Date: 19 May 2020

Revised Date: 25 June 2020

Accepted Date: 29 June 2020

Please cite this article as: Rudski L, Januzzi JL, Rigolin VH, Bohula EA, Blankstein R, Patel AR, Bucciarelli-Ducci C, Vorovich E, Mukherjee M, Rao SV, Beanlands R, Villines TC, Di Carli MF, Multimodality Imaging in Evaluation of Cardiovascular complications in Patients with COVID-19, *Journal of the American College of Cardiology* (2020), doi: https://doi.org/10.1016/j.jacc.2020.06.080.

Multimodality Imaging in Evaluation of Cardiovascular complications in Patients with COVID-19

Brief title: Cardiovascular Imaging in Evaluation of COVID-19 Complications

Expert panel from the American College of Cardiology (ACC) Cardiovascular Imaging Leadership Council

Lawrence Rudski, MD, James L. Januzzi, MD, Vera H. Rigolin, MD, Erin A. Bohula, MD, DPhil, Ron Blankstein, MD, Amit R. Patel, MD, Chiara Bucciarelli-Ducci, MD, PhD, FESC, FRCP, Esther Vorovich, MD, MSCE, Monica Mukherjee, MD, MPH, Sunil V. Rao, MD, FSCAI, Rob Beanlands, MD, Todd C. Villines, MD, Marcelo F. Di Carli, MD

Jewish General Hospital, McGill University, Montreal, Canada (LR)
Massachusetts General Hospital, Harvard Medical School, Boston, MA (JLJ)
Northwestern University Feinberg School of Medicine, Chicago, IL (VR, EV)
Brigham and Women's Hospital, Harvard Medical School, Boston, MA (EAB, RB, MDC)
University of Chicago, Chicago, IL (AP)
Bristol Heart Institute, University of Bristol, Bristol, UK (CBD)
Johns Hopkins University, Baltimore, MD (MM)
Duke University Health System, Durham, NC (SVR)
Ottawa Heart Institute, Ottawa, Canada (RB)
University of Virginia Health System, Charlottesville, VA (TV)

Author Disclosures:
Dr. Januzzi is a Trustee of the American College of Cardiology, is a Board member of Imbria Pharmaceuticals, has received grant support from Novartis Pharmaceuticals and Abbott Diagnostics, consulting income from Abbott Diagnostics, Janssen, Novartis, and Roche Diagnostics, and participates in clinical endpoint committees/data safety monitoring boards for Abbott, AbbVie, Amgen, CVRx, Janssen, and Takeda.
Dr. Patel received research grants from General Electric and Philips.
Dr. Rudski has minor stock holdings in General Electric outside of a managed portfolio.
Dr. Vorovich is on the speakers bureau for Abiomed
Dr. Bohula has received institutional grant support from Amgen, Novartis, Astra Zeneca, Eisai, and The Medicines Company, and consults for Kowa, Novo Nordisk, Amgen, and Medscape.
Dr. Bucciarelli-Ducci receives supported from the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the UK National Institute for Health Research or the UK Department of Health and Social Care.
Dr. Di Carli has received institutional grant support from Gilead Sciences and Spectrum Dynamics, and consulting income from Janssen and Bayer.
Dr. Blankstein has received research support from Amgen Inc. and Astellas Inc.
Dr. Rao has received insitutional research grants from Svelte Inc, Shockwave Medical, and Bayer.
Dr. Mukherjee has no disclosures.
Dr. Rigolin has no disclosures.

Dr. Villines has no disclosures.
Dr. Beanlands has received research grants and consulting honoraria from Lantheus Medical Imaging, Jubilant DraxImage, and GE Healthcare.

Address for correspondence:
Marcelo F. Di Carli, MD
Brigham and Women's Hospital, ASB-L1 037C
75 Francis St, Boston, MA 02115
E-mail: mdicarli@bwh.harvard.edu
Tel: 617-732-6290
Fax: 617-582-6056
Twitter: @mdicarli; @JJheart_doc

Abstract
Standard evaluation and management of the patient with suspected or proven cardiovascular complications of COVID-19, the disease caused by severe acute respiratory syndrome–related coronavirus-2 (SARS-CoV-2), is challenging. Routine history, physical examination, laboratory testing, electrocardiography and plain x-ray imaging may often suffice for such patients but given overlap between COVID-19 and typical cardiovascular diagnoses such as heart failure and acute myocardial infarction, need frequently arises for advanced imaging techniques to assist in differential diagnosis and management. This document provides guidance in several common scenarios among patients with confirmed or suspected COVID-19 infection and possible cardiovascular involvement, including chest discomfort with electrocardiographic changes, acute hemodynamic instability, newly-recognized left ventricular dysfunction, as well as imaging during the sub-acute/chronic phase of COVID-19. For each, we consider the role of biomarker testing to guide imaging decision-making, provide differential diagnostic considerations, and offer general suggestions regarding application of various advanced imaging techniques.

Condensed Abstract: Standard evaluation and management of the patient with suspected or proven cardiovascular complications due to COVID-19 infection often requires advanced imaging techniques to assist in differential diagnosis and management. This document provides guidance in several common scenarios among patients with COVID-19 infection and for each provides advice regarding the role of biomarker testing to guide imaging decision-making, provides differential diagnostic considerations, and offers general suggestions regarding application of various advanced imaging techniques.

Keywords: COVID-19, myocardial injury, stress cardiomyopathy, myocarditis

Abbreviations
ECG = electrocardiogram
CAD = coronary artery disease
ICU = intensive care unit
ARDS = adult respiratory distress syndrome
POCUS = point of care ultrasound
ACS = acute coronary syndrome
LVEF = left ventricular ejection fraction
CTA = computed tomography angiography
MRI = magnetic resonance imaging
SPECT = single photon emission computed tomography
PET = positron emission tomography
VTE = venous thrombotic events
STEMI = ST-segment elevation myocardial infarction
EMB = endomyocardial biopsy
RV = right ventricle

Introduction

Imaging is essential in the diagnosis and risk stratification of disease and in guiding management. The traditional "five-fingered approach" of history, physical exam, blood tests, electrocardiogram (ECG) and imaging is still relevant, but in the COVID-19 era, there are additional challenges due to significant overlap between coronavirus and typical cardiac presentations. For example, among those with COVID-19, chest discomfort is common and ECG and cardiac troponins are frequently abnormal in the absence of obstructive coronary artery disease (CAD), especially among those with severe infections requiring ICU admission (1-3). As well, dyspnea is among the most common symptoms in COVID-19, and B-type natriuretic peptide and chest x-ray are also frequently abnormal in affected patients. Therefore, there is a need for guidance on discriminating significant cardiac pathology from findings which may be associated with COVID-19 infection.

The purpose of this document is to provide a summary of the evidence regarding the prevalence and significance of abnormal findings that may suggest the need for cardiac imaging and to provide expert guidance on incorporating advanced imaging into clinical pathways in suspected or confirmed COVID-19 patients.

Methodology

This guidance document was commissioned by the leadership of the American College of Cardiology (ACC) Cardiovascular Imaging Leadership Council. The writing group for this document was organized to ensure diversity of perspectives and expertise including multimodality cardiovascular imaging, critical care cardiology, heart failure, interventional cardiology and general cardiology. The work of the writing group was supported exclusively by the ACC and specialty imaging societies without commercial support.

In order to maximize the clinical utility of this guidance document, description of imaging findings and relative utility of imaging tests is organized by the most common clinical scenarios requiring expert cardiac consultation described to-date. The writing group realizes that these clinical scenarios are not static and many overlap, but this format allowed to describe better the differential diagnoses and the evolving role of non-invasive imaging tests in guiding management of patients affected by COVID-19. The writing group also recognizes that some of these initial recommendations will likely evolve with increasing knowledge regarding the pathobiology of cardiac complications from SARS-CoV-2 infection and the potential impact of novel therapies that are currently being evaluated on the natural history of the disease. It is also important to recognize that this guidance regarding the relative utility of imaging tests in specific clinical scenarios should be interpreted and adopted in the context of local availability and expertise.

COVID-19 Testing and Implications for Imaging

Diagnostic testing to identify persons infected with SARS–CoV-2 plays a crucial role in protection of healthcare personnel and guiding disinfection of imaging rooms and equipment used in patients with suspected or confirmed COVID-19 infection. The diagnostic sensitivity of reverse transcriptase polymerase chain reaction (RT-PCR)–based assays of respiratory specimens is reported to range between 89% and 96% (range 78-100%) depending on the sample source (4). The information has important implications for protection of healthcare personnel involved in imaging studies and for disinfection of imaging rooms and equipment after their used in patients who are confirmed COVID-19 positive and those who are RT-PCR negative but still considered high-risk for COVID-19. Strict adherence to local infection control policies and procedures is required to minimize exposure and transmission of SARS-CoV-2 to healthcare

staff and patients without COVID-19 referred for imaging. Specific recommendations regarding the use of personal protective equipment (PPE) have been provided by all subspecialty imaging societies (5-8).

Role of Biomarkers to Inform Imaging Decision-Making in COVID-19

Measurement of circulating biomarkers to support clinical judgment in patients with COVID-19 has grown because many circulating biomarkers reflecting end-organ stress/injury, inflammation, hypo-perfusion, and pathway activation of thrombosis/hemostasis have been found to have prognostic value in patients with COVID-19 (**Table 1**), predicting longer hospital stay, need for ICU admission, onset of ARDS, and risk for death (2,9-18). However, despite a prognostic role, almost none of the widely measured biomarkers represent a specific trigger for imaging outside of that supported by clinical judgment.

Cardiac-derived biomarkers reflecting myocardial stress (B-type natriuretic peptide [BNP] and N-terminal pro-BNP [NT-proBNP]) and myocardial injury (cardiac troponin, cTn) are both strongly prognostic in COVID-19 (2,10-13,15,16), particularly in patients with rising values during hospitalization and in those with marked biomarker elevation (12). Importantly, clinicians should be aware that most patients with abnormal BNP/NT-proBNP or cTn do not have acute heart failure or myocardial infarction and rise in concentration of either class of biomarker presumably reflects complex processes including direct myocardial stress/injury related to systemic illness. To the extent cardiac dysfunction is a major adverse prognostic finding in COVID-19, links between BNP/NT-proBNP and cTnT or I with myocardial dysfunction make it tempting to regard them as a valuable tool for decision-making regarding need for imaging.

Accordingly, when interpreted within the context of the entire clinical picture, low-modest and non-rising concentrations of either class of biomarker may help to exclude need for imaging. In those with marked elevation (e.g., severe heart failure, myocardial infarction or myocarditis), selective imaging might be considered if clinical judgment dictates. Of course, both classes of biomarkers retain their usefulness for diagnosis of acute heart failure or type 1 myocardial infarction in patients with concomitant acute cardiac issues and co-morbid COVID-19.

Clinical Presentations

A typical presentation of the COVID-19 positive or possible patient is dyspnea with a chest x-ray demonstrating interstitial or airspace infiltrates suggestive of pneumonia (19). The clinician may be consulted to rule in or rule out a cardiogenic component of pulmonary abnormalities in this symptomatic patient population. Clinicians will rely on history, physical exam, ECG and biomarkers, and recent cardiac imaging tests if available. Underlying cardiac history including CAD, cardiomyopathy, heart failure, and arrhythmia should be sought, and frequent contributors to decompensation should be eliminated (20). As discussed below, the additional use of cardiac imaging may be helpful in the evaluation of cardiac complications from COVID-19. However, given the higher risk of exposure of healthcare personnel imaging studies should be used carefully and only in clinical situations where their use can inform a change in patient management. The writing group agreed that either a point of care ultrasound (POCUS) or a formal limited echocardiogram may be considered as the initial evaluation of positive or suspected COVID-19 patients with possible cardiac injury (21). Advanced imaging techniques may also play an important role, which will be discussed under the specific clinical scenarios discussed below.

Clinical Scenario 1: Chest pain and abnormal ECG

Typical findings and differential diagnosis

Chest discomfort is a common symptom among patients with active COVID-19 infection and may result from a large number of etiologies (**Table 2**).

Initial Diagnostic Approach

The initial diagnostic evaluation of patients presenting with chest pain is illustrated in **Figure 1**. The 12-lead ECG and biomarkers play a key role. In addition to concern for traditional acute coronary syndromes (ACS) (ST-elevation ACS or non-ST-elevation ACS), patients with active COVID-19 infection have been reported to present with ECG abnormalities later shown to be related to one or more of the conditions outlined in **Table 2** (22,23). In patients with atypical symptoms for traditional ACS or non-typical ECG changes, rapid access to cardiovascular imaging may provide important diagnostic information to guide management.

- Patients with chest pain and clinical concern for ST-elevation ACS or high clinical risk for in-hospital mortality (e.g., cardiogenic shock, LVEF <40% felt due to NSTEMI, dynamic ST-segment changes), should be referred for emergent coronary angiography and reperfusion therapy (24) (**Figure 2**).
- In patients with equivocal symptoms, atypical or equivocal ECG abnormalities, or late presentation, clinicians may consider POCUS or limited echocardiogram to assess for regional wall motion abnormalities and LVEF and/or coronary CTA as discussed below (8,24).

Role of Advanced Imaging Techniques

In patients with *chest pain and ST-elevation without clear evidence of STEMI,* coronary CTA is preferred as an initial advanced imaging study in order to rule out ACS (25) and point to

alternate diagnoses discussed in Clinical Scenarios 2 and 3, especially in patients in whom a diagnostic quality study can be obtained. Patients need to be able to participate in breath holding and achieve reasonable heart rate control and should not have contraindications to iodinated contrast administration. Coronary CTA is particularly useful in patients without previously established CAD or severe coronary artery calcification.

In patients with a *clinical presentation of acute MI, normal or non-obstructive coronary arteries (MINOCA)*, which may present as STEMI or NSTEMI, with normal or abnormal LV systolic function, cardiac MRI can help confirm the diagnosis of MI or provide alternate diagnosis including myocarditis, stress cardiomyopathy, and embolic infarction (26) (**Table 2, Figure 2, Supplemental Table 3**). A patient without evidence of obstructive CAD by angiography and an echocardiogram demonstrating a pattern consistent with stress cardiomyopathy may not need additional imaging, particularly if a repeat study shows resolution of dysfunction. However, when the presentation is atypical or there is diagnostic uncertainty, cardiac MRI can help identify the mechanism of myocardial dysfunction.

In *hemodynamically stable patients with previously established CAD* presenting with chest pain of unclear etiology in whom a non ST elevation ACS is a consideration, pharmacologic stress imaging is the preferred non-invasive approach (**Figure 2**), although in low risk ACS, testing might be deferred until after COVID-19 resolution.

There are several important considerations when selecting among available functional stress imaging tests. Exercise stress testing, including exercise echocardiography (5), should be generally avoided in patients with confirmed or suspected active COVID-19 infection due to the potential risk of aerosolizing droplets. Vasodilator stress myocardial perfusion imaging (MPI) with SPECT, PET or MRI are all options to consider. If available, stress MPI with PET or MRI,

or stress-first approach with SPECT especially in patients with BMI < 30 and without known CAD would be preferred because of the short protocol times (generally 20-45 min), which limit exposure to staff. Dobutamine-stress echocardiography is an option if radionuclide imaging or MRI are not available.

Clinical Scenario 2: Hemodynamic Instability (shock or hypotension)

Typical findings and differential diagnosis

Patients with COVID-19 may manifest with hemodynamic instability with a wide range of abnormalities, including LV and/or RV dysfunction with regional or global abnormalities, with or without myocardial injury, and with or without evidence of myocarditis (1,22,27-30). Imaging findings typically associated with chronic cardiac conditions such as LVH and LV dilatation, have been well described in acute cardiac presentations of COVID-19 patients and have demonstrated significant reversibility and may not be reliable markers to judge chronicity of cardiac dysfunction (31).

While the pulmonary manifestations predominate in most patients with COVID-19, involvement of other organs is common with acute cardiac injury occurring in up to 28% and venous thrombotic events (VTE) in up to 67% (32-34). Cardiogenic shock has been reported as the first manifestation of COVID-19 in the absence of respiratory symptoms (1). As such, clinicians should have a high degree of suspicion for COVID-19 in the setting of hemodynamic instability even if the patient is not presenting with its classic constellation of symptoms.

Hemodynamic instability includes shock, which is classically divided into several physiologic categories: distributive, obstructive, hypovolemic, and cardiogenic (35). Cardiogenic shock can further be subdivided into classic cardiogenic shock, defined by low cardiac output, high filling pressures and high systemic vascular resistance, and mixed (or

vasodilatory) cardiogenic shock. Distributive or septic shock was observed commonly (~20% of hospitalized COVID-19 patients) in early reports from China (19). While the incidence of heart failure or cardiogenic shock is not well defined, early estimates described rates as high as 30-50% in patients requiring ICU-care or non-survivors (19,27).

The potential mechanisms of direct myocardial dysfunction leading to hemodynamic instability in patients with COVID-19 are numerous (**Table 2**) (32). The underlying pathologic mechanisms of the clinical syndrome of myocarditis remain unclear and may include direct viral toxicity, microvascular dysfunction due to microthrombosis, vasculitis, vascular injury, or lymphocytic infiltration (30,32).

Initial Diagnostic Approach

Initial evaluation of the patient with hemodynamic instability should include all elements outlined in **Figure 1**. The physical exam should focus on an assessment of congestion, perfusion and be geared towards identification of cardiogenic or mixed shock. Initial testing should include markers of perfusion (e.g., lactate, liver function tests, renal function), and may include measurement of BNP/NT-proBNP, cTn, coagulation and inflammatory markers and an assessment of cardiac output.

In the setting of a clear STEMI with hemodynamic instability, it is recommended to proceed directly to coronary angiography and reperfusion therapy without the need of additional imaging (**Figure 3**), as described in Clinical Scenario 1 (24).

In patients with hemodynamic instability, evidence of significant/worsening myocardial injury, or ECG abnormalities without clear evidence of STEMI, assessment with POCUS is recommended (**Figure 3, Supplemental Tables 1-3**). This may help guide the decision on whether to proceed with coronary evaluation, although it is noteworthy that myocarditis and

myocardial injury may also present with regional wall motion abnormalities. In the absence of a high pre-test probability of acute MI (type 1), coronary CTA may be useful to minimize staff exposure (8,24).

Role of Advanced Imaging Techniques

If acute epicardial CAD is ruled out or the suspicion for ACS is low, it is reasonable to consider further evaluation for myocarditis or stress cardiomyopathy (**Figure 3, Supplemental Table 3**), if such information may lead to a change in patient management.

There should be a high index of suspicion for pulmonary embolism in confirmed or suspected COVID-19 patients, particularly in those with hemodynamic instability, unexplained sinus tachycardia or evidence of RV strain by ECG or echocardiogram or rising d-dimer. A contrast-enhanced chest CT is the imaging modality of choice (**Figure 3**). RV dysfunction is nonspecific and may also be observed in other high RV afterload states, such as with hypoxic pulmonary vasoconstriction or high PEEP in mechanically ventilated patients.

The role of endomyocardial biopsy (EMB) in COVID-19 associated cardiogenic shock remains unclear. Recommendations for the use of EMB in patients presenting with unexplained acute cardiomyopathy and (36) are based on clinical presentations in which EMB results would change treatment or to assist in prognostication (37,38). Given no clear therapy exists for COVID-19 related myocarditis and risks of personnel exposure during the procedure, use of EMB should be reserved for patients in whom such results would change management course.

Clinical Scenario 3: New Left Ventricular Dysfunction Without Shock or Hypotension

Typical findings and differential diagnosis

As noted above, myocardial stress and injury, as reflected by abnormal concentrations of BNP/NT-proBNP or cTn, are common in patients with COVID-19 (27,39). The clinical

presentation of LV dysfunction (LVD) in COVID-19 is quite heterogeneous ranging from incidentally discovered LVD with negative biomarkers to mild symptomatic LVD to a clinical picture of fulminant myocarditis and shock (**Table 2**). Systolic dysfunction can present as either regional wall motion abnormalities that may or may not fit a coronary artery distribution to various forms of stress cardiomyopathy including classic and atypical patterns to severe global systolic dysfunction with hemodynamic instability (**Figure 4**).

Acute coronary syndrome should be considered in patients presenting with typical clinical, ECG and echocardiographic features. Distinguishing between acute and chronic LVD in COVID-19 can be difficult as multiple features overlap (**Figure 4**). The presence of a non-dilated LV on echocardiography, particularly in the context of significantly elevated/rising biomarker concentrations, profound systolic dysfunction and/or LVH and significant heart failure or hemodynamic instability suggests an acute pathophysiology. In contrast, presentation of a severely dilated LV, left atrial enlargement, thinned or akinetic walls and low or stable cTn suggest a pre-existing chronic cardiomyopathy. The presence of myocardial inflammation/edema by cardiac MRI or PET can be useful in distinguishing acute from chronic LVD.

COVID-19 myocarditis diagnosed by combination of cardiac MRI and myocardial injury has been described both in patients with normal (40) or abnormal LV function (1). A thickened LV wall that regresses within 4-7 days is a common anecdotal finding described in case reports(1,28,29), which may represent extensive myocardial edema (1,29) and frequently associated with low voltage on ECG.

Initial Diagnostic Approach

Initial evaluation should include all elements outlined in **Figure 1**. In addition to standard chest X-ray and ECG, biomarker testing may be useful to identify acute myocardial stress or injury as discussed above and noted in **Table 1** and **Figure 4**. The use of limited versus full echocardiography may depend on the differential diagnoses that are being considered (**Table 2**) and level of diagnostic information needed (**Supplemental Table 1**).

Role of Advanced Imaging Techniques

In patients with known or suspected structural heart disease during the initial POCUS, additional echocardiographic imaging should be considered to further characterize such findings (**Figure 4, Supplemental Tables 1 and 3**). Transesophageal echocardiography (TEE) is an aerosol generating procedure and should be avoided if possible during the acute phase of COVID-19 (5). In selected cases, cardiac CT may be useful and minimize exposure of healthcare personnel (8).

The use of advanced imaging tests to evaluate for suspected ACS, chronic CAD, or other forms of myocardial injury in patients presenting with LV dysfunction should follow recommendations discussed in Clinical Scenarios 1 and 2 (**Figure 4**). When there is a suspicion for myocarditis and cardiac MRI is equivocal or cannot be performed, cardiac PET may provide information on the presence of cardiac inflammation(41). As discussed above, EMB may be considered in selected patients presenting with Clinical Scenarios 2 or 3 (**Figure 4**).

Clinical Scenario 4: Subacute/chronic phase

Typical findings and Differential Diagnosis

Many of the sub-acute and chronic findings in COVID-19 cardiovascular disease are non-specific and may include symptoms such as dyspnea, fatigue, weakness, or cough. More concerning cardiac symptoms include chest pain, syncope, pre-syncope, or palpitations, and new

signs of heart failure. The long term consequences and prognosis of myocardial damage incurred during COVID-19 are unknown. However, following the initial SARS-CoV-1 epidemic in 2002, chronic cardiac and pulmonary manifestations were reported after recovery (18,42) and it is reasonable to expect the same with SARS-CoV-2.

The differential diagnosis should include COVID-19 related and non-COVID-19 related etiologies (**Table 2**). Non-COVID-19 related etiologies should be evaluated in standard fashion. COVID-19 related etiologies may include deconditioning, recovery from illness, residual lung disease, and manifestations of various forms of cardiovascular disease. Cardiovascular sequalae from acute COVID-19 may include arrythmias, left and right ventricular dysfunction and heart failure, or ischemic heart disease. Both supraventricular and ventricular arrythmias may appear in the sub-acute and chronic phases and may present as palpitations, heart failure, chest pain, presyncope or syncope.

Initial Diagnostic Approach

Initial evaluation should include all elements outlined in **Figure 1**. The utility of serum biomarkers is undefined in the subacute/chronic phase. It is reasonable to suspect that elevated concentrations of BNP/NT-proBNP in a dyspneic post-COVID-19 patient might be helpful to understand presence and severity of cardiac dysfunction or clinical heart failure and such biomarkers should be utilized in accordance with published clinical practice guidelines (43).

Role of Advanced Imaging Techniques

New signs of heart failure / persistent dyspnea out of proportion to lung disease

The evaluation of patients presenting persisting or new dyspnea should follow the same considerations outlined in Clinical Scenario 3. If there is any concern for development of pulmonary hypertension, particularly chronic thromboembolic pulmonary hypertension

(CTEPH), the patient should be referred to an appropriate specialist and a right heart catheterization can be considered.

Known LV dysfunction (during acute phase)

If the patient was diagnosed with new LV dysfunction in the hospital, repeat echocardiogram (or MRI) at 2-6 months following discharge to assess for myocardial recovery may be considered. Guideline directed medical therapy should be optimized (43).

New syncope / significant palpitations

These patients should undergo evaluation of syncope and arrhythmias as defined in current guidelines, which include consideration of advanced imaging to assess for CAD, scar and ischemia (44).

Chest discomfort

These patients should undergo evaluation of ischemic heart disease as defined in current guidelines, which include consideration of advanced non-invasive imaging and coronary angiography (45,46).

Summary and Conclusions

The management of cardiovascular complications in patients with COVID-19 presents substantial diagnostic and therapeutic challenges. Selective use of advanced cardiac imaging offers powerful qualitative and quantitative information that can help with patient management (**Central Illustration**). Below are the key summary points from this expert panel guidance regarding the use of multimodality imaging in COVID-19 patients:

- TTE is usually the initial cardiovascular imaging modality used to guide management. This may be in the form of an urgent POCUS or a limited study initially. More complete studies are guided by the clinical question and evolving patient condition.

- Clear or suspected STEMI usually mandates emergent cardiac catheterization with limited role for noninvasive imaging. Less typical presentations of potential acute coronary syndrome may benefit from a POCUS and coronary CT angiography. In patients with MINOCA, cardiac MRI can be useful in distinguishing the etiology of myocardial injury.
- In patients with known CAD with suspected low risk ACS, vasodilator stress MRI or radionuclide MPI, especially PET if available, can be considered.
- In patients with new LV systolic dysfunction, consideration of underlying CAD should be investigated. For those without evidence of CAD, cardiac MRI or PET can provide important insights into the etiology of myocardial dysfunction.
- In the sub-acute phase, surveillance of previously detected abnormalities is important to follow for potential recovery (as in Takotsubo cardiomyopathy or myocarditis) or progressive disease.
- In all scenarios, consideration of risk to the health care workers is an integral part of the decision-making process. Decision to pursue additional imaging should be based on the assumption that the results will change patient management.
- Individual institutions must rely on local expertise and resources to determine access to testing and imaging must be consistent with goals of treatment.

Highlights

- COVID-19 infections frequently associate with cardiac injury, which increases the risk of morbidity and mortality.
- Advanced imaging facilitate diagnosis but should be used to inform a change in management.

The impact of imaging on patient management during the chronic phase of COVID-19 warrants additional investigation.

References

1. Inciardi RM, Lupi L, Zaccone G et al. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol 2020.

2. 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.

3. Akhmerov A, Marban E. COVID-19 and the Heart. Circ Res 2020;126:1443-1455.

4. Tu YP, Jennings R, Hart B et al. Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. N Engl J Med 2020.

5. Kirkpatrick J, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak. 2020.

6. Han Y, Chen T, Bryant J et al. Society for Cardiovascular Magnetic Resonance (SCMR) guidance for the practice of cardiovascular magnetic resonance during the COVID-19 pandemic. J Cardiovasc Magn Reson 2020 2020;22:26.

7. Skali H, Murthy VL, Al-Mallah MH et al. Guidance and Best Practices for Nuclear Cardiology Laboratories during the Coronavirus Disease 2019 (COVID-19) Pandemic: An Information Statement from ASNC and SNMMI. 2020.

8. Choi AD, Abbara S, Branch KR et al. Society of Cardiovascular Computed Tomography guidance for use of cardiac computed tomography amidst the COVID-19 pandemic Endorsed by the American College of Cardiology. J Cardiovasc Comput Tomogr 2020.

9. Chen G, Wu D, Guo W et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020;130:2620-2629.

10. Chen T, Wu D, Chen H et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091.

11. Gao L, Jiang D, Wen XS et al. Prognostic value of NT-proBNP in patients with severe COVID-19. Respir Res 2020;21:83.

12. Guo T, Fan Y, Chen M et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol 2020.

13. Han H, Xie L, Liu R et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. J Med Virol 2020.

14. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 2020.

15. Li JW, Han TW, Woodward M et al. The impact of 2019 novel coronavirus on heart injury: A Systematic review and Meta-analysis. Prog Cardiovasc Dis 2020.

16. Santoso A, Pranata R, Wibowo A, Al-Farabi MJ, Huang I, Antariksa B. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: A meta-analysis. Am J Emerg Med 2020.

17. Thachil J, Tang N, Gando S et al. Laboratory haemostasis monitoring in COVID-19. J Thromb Haemost 2020.

18. Zhang L, Yan X, Fan Q et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost 2020.

19. 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;395:1054-1062.

20. Hollenberg SM, Warner Stevenson L, Ahmad T et al. 2019 ACC Expert Consensus Decision Pathway on Risk Assessment, Management, and Clinical Trajectory of Patients Hospitalized With Heart Failure: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2019;74:1966-2011.

21. Spencer KT, Kimura BJ, Korcarz CE, Pellikka PA, Rahko PS, Siegel RJ. Focused cardiac ultrasound: recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr 2013;26:567-81.

22. Bangalore S, Sharma A, Slotwiner A et al. ST-Segment Elevation in Patients with Covid-19 - A Case Series. N Engl J Med 2020.

23. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA Cardiol 2020.

24. Mahmud E, Dauerman HL, Welt FG et al. Management of Acute Myocardial Infarction During the COVID-19 Pandemic. J Am Coll Cardiol 2020.

25. Linde JJ, Kelbaek H, Hansen TF et al. Coronary CT Angiography in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. J Am Coll Cardiol 2020;75:453-463.

26. Tamis-Holland JE, Jneid H, Reynolds HR et al. Contemporary Diagnosis and Management of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease: A Scientific Statement From the American Heart Association. Circulation 2019;139:e891-e908.

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

28. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J 2020.

29. Sala S, Peretto G, Gramegna M et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J 2020.

30. Tavazzi G, Pellegrini C, Maurelli M et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. Eur J Heart Fail 2020.

31. Zagrosek A, Wassmuth R, Abdel-Aty H, Rudolph A, Dietz R, Schulz-Menger J. Relation between myocardial edema and myocardial mass during the acute and convalescent phase of myocarditis--a CMR study. J Cardiovasc Magn Reson 2008;10:19.

32. Atri D, Siddiqi HK, Lang J, Nauffal V, Morrow DA, Bohula EA. COVID-19 for the Cardiologist: A Current Review of the Virology, Clinical Epidemiology, Cardiac and Other Clinical Manifestations and Potential Therapeutic Strategies. JACC Basic Transl Sci 2020.

33. Klok FA, Kruip M, van der Meer NJM et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020.

34. Llitjos JF, Leclerc M, Chochois C et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost 2020.

35. van Diepen S, Katz JN, Albert NM et al. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. Circulation 2017;136:e232-e268.

36. Kociol RD, Cooper LT, Fang JC et al. Recognition and Initial Management of Fulminant Myocarditis: A Scientific Statement From the American Heart Association. Circulation 2020;141:e69-e92.

37. Bennett MK, Gilotra NA, Harrington C et al. Evaluation of the role of endomyocardial biopsy in 851 patients with unexplained heart failure from 2000-2009. Circ Heart Fail 2013;6:676-84.

38. Bozkurt B, Colvin M, Cook J et al. Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies: A Scientific Statement From the American Heart Association. Circulation 2016;134:e579-e646.

39. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020.

40. Doyen D, Moceri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. Lancet 2020.

41. Nensa F, Kloth J, Tezgah E et al. Feasibility of FDG-PET in myocarditis: Comparison to CMR using integrated PET/MRI. J Nucl Cardiol 2018;25:785-794.

42. Ong KC, Ng AW, Lee LS et al. Pulmonary function and exercise capacity in survivors of severe acute respiratory syndrome. Eur Respir J 2004;24:436-42.

43. Yancy CW, Jessup M, Bozkurt B et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2017;70:776-803.

44. Al-Khatib SM, Stevenson WG, Ackerman MJ et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2018;72:e91-e220.

45. Fihn SD, Blankenship JC, Alexander KP et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable

ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2014;64:1929-49.

46. Knuuti J, Wijns W, Saraste A et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020;41:407-477.

Figure Legends

Figure 1. Initial diagnostic approach. The initial diagnostic workup includes history & physical exam, ECG, chest x-ray and biomarkers. POCUS or a limited echocardiogram should also be considered in selected clinical presentations.

Figure 2. Role of cardiac imaging in patients presenting chest pain and suspected ACS. Patients with chest pain and clinical concern for ST-elevation ACS or high clinical risk for in-hospital mortality should be referred for emergent coronary angiography and reperfusion therapy. In patients with equivocal symptoms, atypical or equivocal ECG abnormalities, or late presentation, clinicians may consider POCUS or limited echocardiogram to assess for regional wall motion abnormalities and LVEF and/or coronary CTA to rule out ACS and point to alternate diagnoses discussed of acute cardiac injury. In patients with known CAD and equivocal ECG changes, stress imaging may be helpful.

Figure 3. Role of cardiac imaging in patients presenting with hemodynamic instability. After an initial evaluation, patients with clear STEMI with hemodynamic instability should be referred to coronary angiography and reperfusion therapy without additional imaging. In patients with evidence of significant/worsening myocardial injury, or ECG abnormalities without clear evidence of STEMI, assessment with POCUS or formal echocardiogram is recommended to help exclude pericardial effusion/tamponade, valvular pathology and RV dysfunction. Coronary CTA may be useful to exclude an ACS in patients with equivocal ECG changes and abnormal LV function. Cardiac MRI can help differentiate myocarditis from stress cardiomyopathy and can be considered if it is likely to lead to a change in patient management.

Figure 4. Role of cardiac imaging in patients presenting with new LV dysfunction without hemodynamic instability. Acute coronary syndrome should be considered in patients presenting

with typical clinical and ECG features and, if present, should be referred to emergent coronary angiography and reperfusion therapy. Distinguishing between acute and chronic LVD in COVID-19 in patients without ACS can be difficult as multiple features overlap. Echocardiography, coronary CTA, cardiac MRI, and ischemia testing can be considered depending on initial clinical findings.

Central Illustration: This figure show the various imaging questions that may present in various stages of COVID-19 disease. The x-axis depicts time. As the disease progress, patient may evolve from having acute disease to a convalescent phase and then chronic disease. The four red boxes highlight the various clinical scenarios. The organ boxes list some of the pathological processes that are being evaluated in each scenario. STEMI= ST segment elevation myocardial infarction; ECG=electrocardiogram ; MRI= magnetic resonance imaging ; VTE= venous thromboembolism.

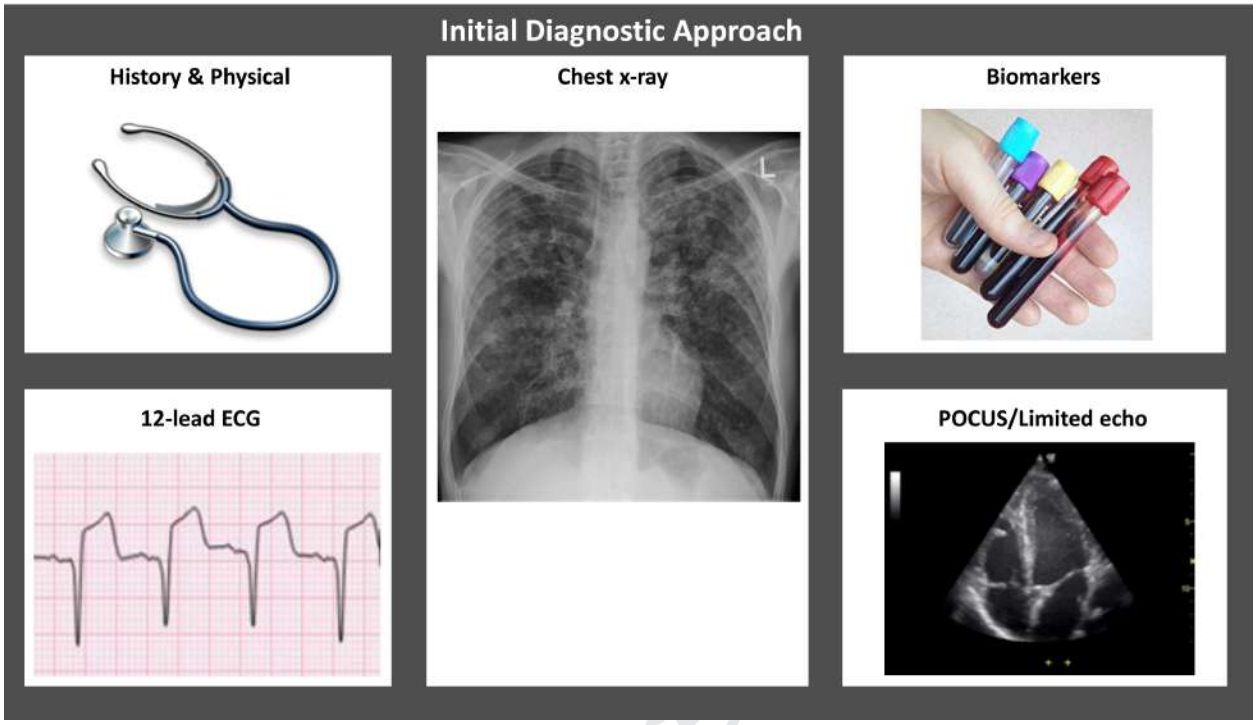
Table 1: Frequently measured prognostic circulating biomarkers in COVID-19. When elevated or rising, these biomarkers provide incremental information regarding outcome, but may not necessarily identify an actionable process.

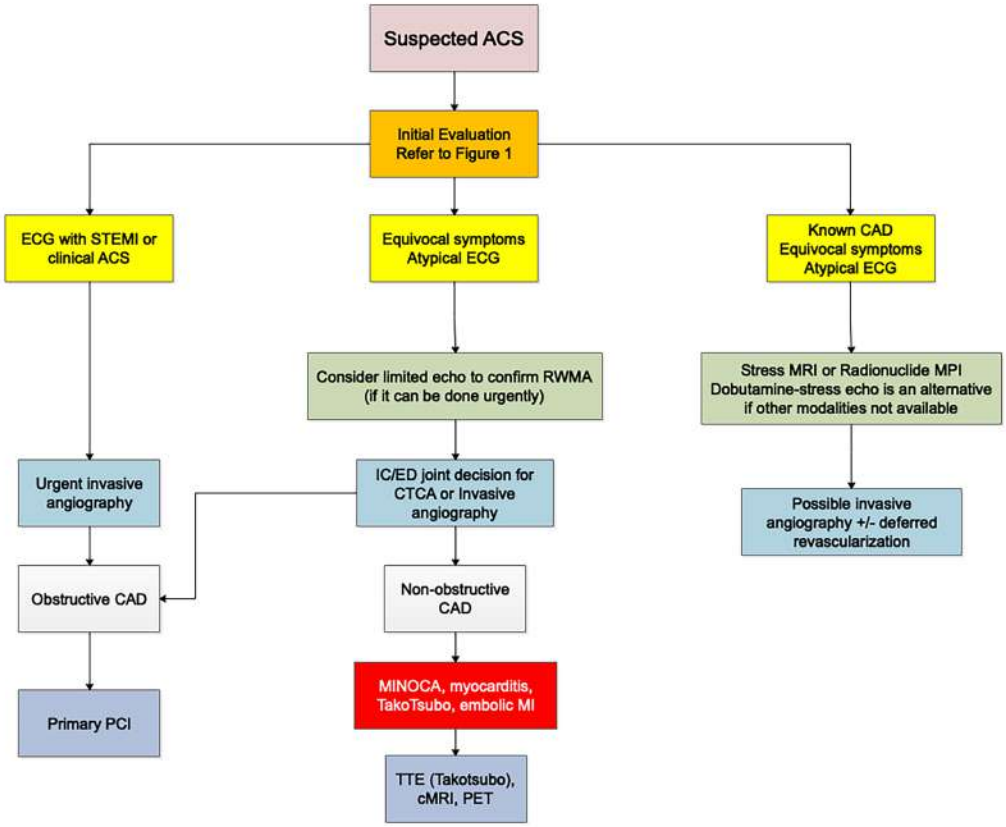
General chemistry	• Alanine/Aspartate aminotransferase • Bilirubin • Creatinine • Lactate • Lactate dehydrogenase
Cell counts	• Leukocyte count (leukocytosis with lymphopenia) • Platelet count (thrombocytopenia)
Inflammatory/acute phase markers	• C-reactive protein • Ferritin • Interleukin-6 • Procalcitonin
Thrombosis/hemostasis	• D-dimer
Cardiac markers	• B-type natriuretic peptide • N-terminal pro-B type natriuretic peptide • Troponin T • Troponin I

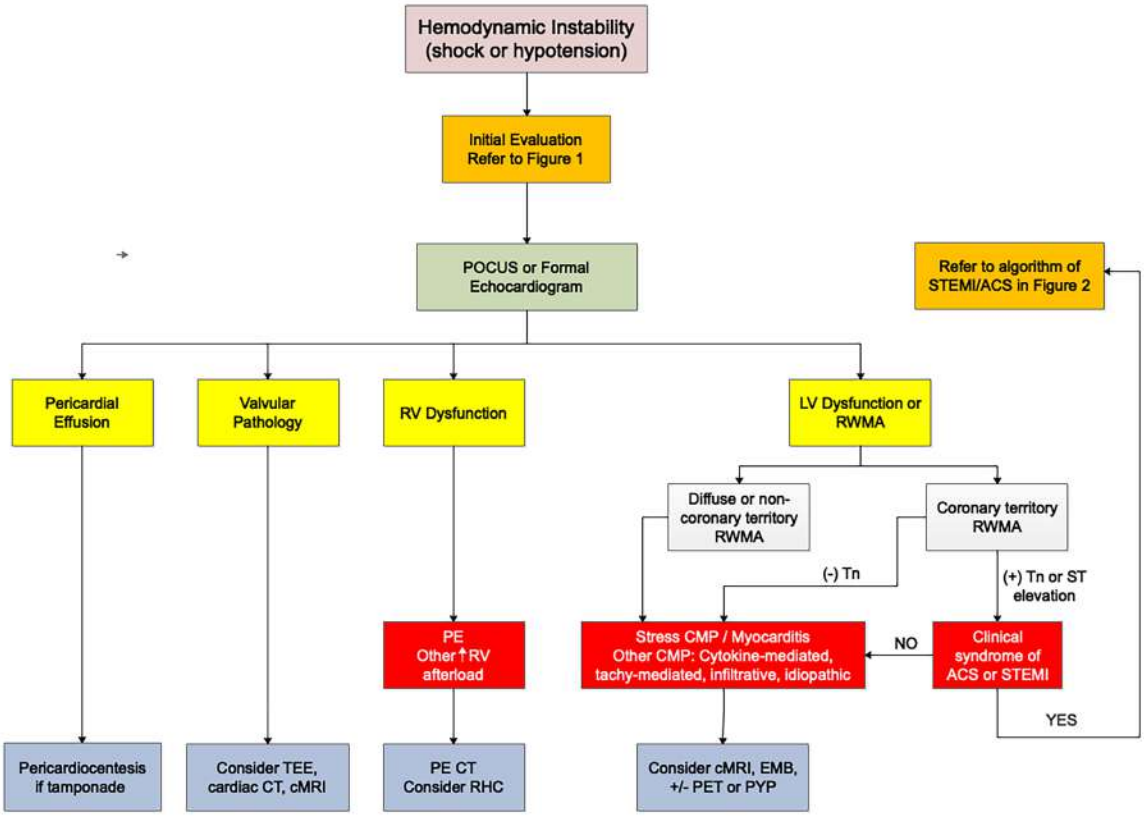
Table 2. Clinical scenarios and differential diagnosis.

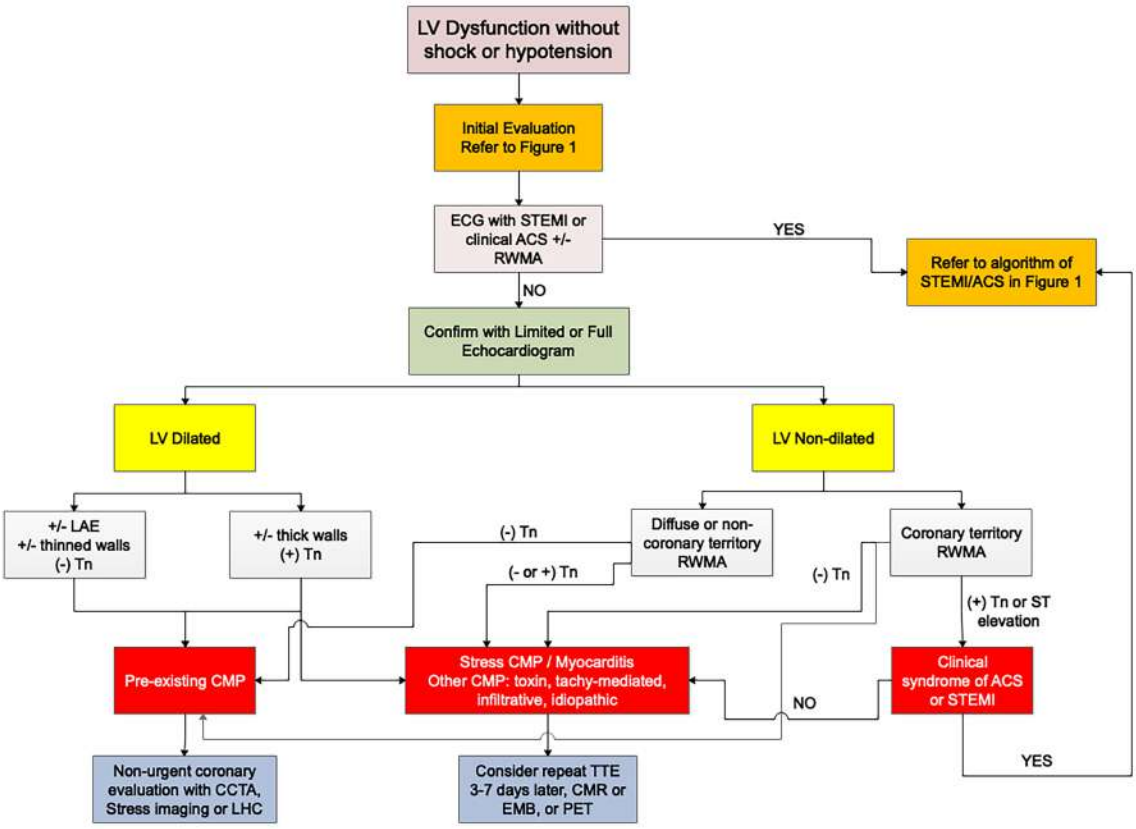
Clinical Scenario	Differential diagnosis
Chest pain with abnormal ECG	• pneumonia • myocarditis • pericarditis • pulmonary embolism • stress cardiomyopathy • myocardial injury related to hypoxemia and tachycardia (severe illness) • acute coronary syndrome
Hemodynamic instability	• Coronary ischemia, with or without acute myocardial infarction • viral myocarditis • stress cardiomyopathy • cytokine mediated cardiomyopathy • pulmonary embolism • pericardial effusion and tamponade • RV dysfunction in the setting of high positive end-expiratory pressure [PEEP] with mechanical ventilation) • arrhythmia • mixed shock in patients with septic

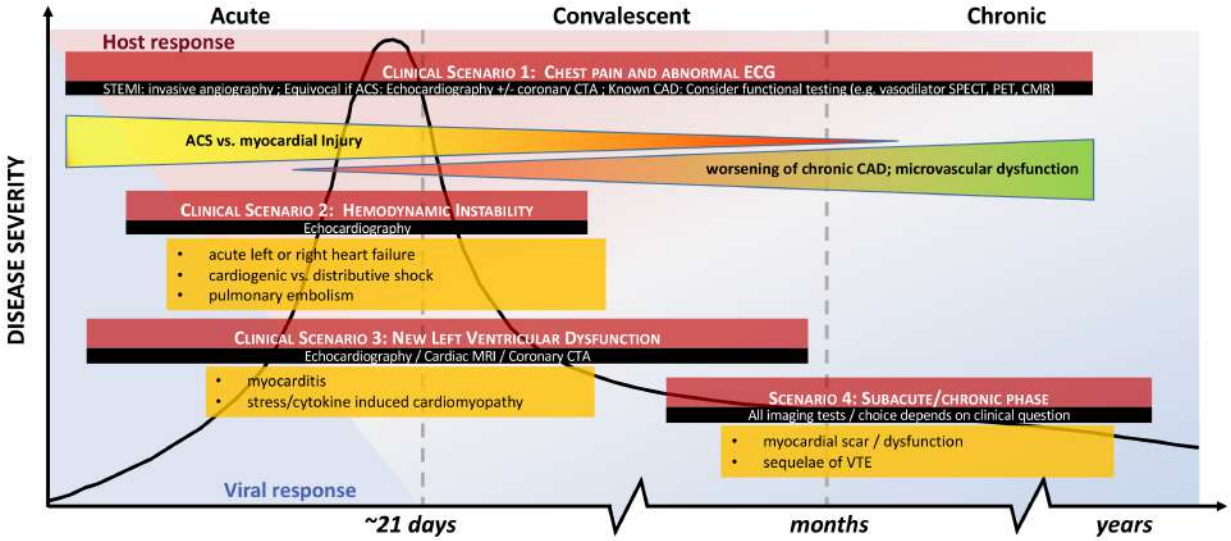
	shock and an inability to compensate due to chronic cardiac dysfunction
New left ventricular dysfunction without hemodynamic instability	• chronic ischemic heart disease • chronic nonischemic cardiomyopathy • acute coronary syndrome • acute/fulminant viral myocarditis, • stress cardiomyopathy • cytokine mediated cardiomyopathy • tachycardia mediated cardiomyopathy • other forms of cardiomyopathy including toxin and infiltrative
Subacute/chronic presentation	• heart failure from volume overload (e.g. from fluid resuscitation during the inpatient stay) or due to decompensation of their new or preexisting cardiomyopathy • ischemic heart disease from progressive coronary or microvascular disease • myocarditis • pulmonary embolism • thromboembolic disease




Suspected ACS
Initial Evaluation
Refer to Figure 1
ECG with STEMI or clinical ACS
Equivocal symptoms
Atypical ECG
Known CAD
Equivocal symptoms
Atypical ECG
Consider limited echo to confirm RWMA (if it can be done urgently)
Stress MRI or Radionuclide MPI
Dobutamine-stress echo is an alternative if other modalities not available
Urgent invasive angiography
IC/ED joint decision for CTCA or Invasive angiography
Possible invasive angiography +/- deferred revascularization
Obstructive CAD
Non-obstructive CAD
Primary PCI
MINOCA, myocarditis, TakoTsubo, embolic MI
TTE (Takotsubo), cMRI, PET


Hemodynamic Instability (shock or hypotension)
Initial Evaluation Refer to Figure 1
POCUS or Formal Echocardiogram
Refer to algorithm of STEMI/ACS in Figure 2
Pericardial Effusion
Valvular Pathology
RV Dysfunction
LV Dysfunction or RWMA
Diffuse or non-coronary territory RWMA
Coronary territory RWMA
(-) Tn
(+) Tn or ST elevation
PE
Other ↑RV afterload
Stress CMP / Myocarditis
Other CMP: Cytokine-mediated, tachy-mediated, infiltrative, idiopathic
NO
Clinical syndrome of ACS or STEMI
YES
Pericardiocentesis if tamponade
Consider TEE, cardiac CT, cMRI
PE CT
Consider RHC
Consider cMRI, EMB, +/- PET or PYP


LV Dysfunction without shock or hypotension
Initial Evaluation Refer to Figure 1
ECG with STEMI or clinical ACS +/- RWMA
YES
Refer to algorithm of STEMI/ACS in Figure 1
NO
Confirm with Limited or Full Echocardiogram
LV Dilated
LV Non-dilated
+/- LAE +/- thinned walls (-) Tn
+/- thick walls (+) Tn
(-) Tn
Diffuse or non-coronary territory RWMA
Coronary territory RWMA
(- or +) Tn
(-) Tn
(+) Tn or ST elevation
Pre-existing CMP
Stress CMP / Myocarditis Other CMP: toxin, tachy-mediated, infiltrative, idiopathic
Clinical syndrome of ACS or STEMI
NO
YES
Non-urgent coronary evaluation with CCTA, Stress imaging or LHC
Consider repeat TTE 3-7 days later, CMR or EMB, or PET



Online Table 1. Echocardiographic approaches to suspected or proven cardiovascular involvement in COVID-19.

Echo Modality	Clinical Scenario	Findings
POCUS	• Chest pain with abnormal ECG • Hemodynamic instability	– Gross LV systolic Function – RV Size/Gross Function – Gross Valve Assessment - 2D/color Doppler – IVC size – Pericardial Effusion
LIMITED TTE	• Chest pain with abnormal ECG • Hemodynamic Instability • Long-term follow-up	– Above plus – LV systolic function and size – Follow-up LV function – e.g. myocarditis, Takotsubo – Regional wall motion assessment – RV size and systolic function acute and follow-up – Valvular assessment as needed – Hemodynamics – e.g. SPAP – Pericardial effusion follow-up
COMPLETE TTE	• Chest pain with abnormal ECG (non emergent setting) • Hemodynamic instability • New LV systolic dysfunction • Long-term follow-up	– Above plus: – Detailed quantification of valvulopathy – Tissue Doppler / diastolic function including LA volume – 2D strain
TEE	• Hemodynamic instability	– Guidance for VA ECMO cannulation and monitoring – Assess aorta – acute aortic syndromes – when unable to perform CT/MRI – Valvulopathy – Endocarditis – when TTE inadequate and will alter management

POCUS = Point of care examination of the cardiovascular system performed by a physician by using ultrasound as an adjunct to the physical examination to recognize specific ultrasonic signs that represent a narrow list of potential diagnoses in specific clinical settings. This is often done on a hand-held system with limited ability to perform detailed assessment and measurements

LIMITED ECHO = A limited examination is usually a follow-up or focused study that does not evaluate all the structures required for a comprehensive or complete echocardiographic exam. The purpose of this exam is best described and documented as a focused clinical exam to answer a specific clinical question. It is assumed that this study is done on a platform capable of full echo assessment

COMPLETE TTE = A complete echocardiogram is one that includes multiple 2D views of all chambers, valves, pericardium, and portions of the aorta, with appropriate measurements. The inability to visualize or measure the clinically relevant anatomy requires documentation of the attempt. Additional anatomy and M mode tracings may not be required but may also be included.

Online Table 2: Limited transthoracic Echo Protocol for COVID-19 Patients

- Parasternal Long axis view
- Parasternal long axis view with color Doppler of the mitral and aortic valves

- Parasternal short axis view at the level of the aortic valve
- Parasternal short axis view at the level of the aortic valve with color Doppler of the tricuspid valve
- Continuous wave Doppler of the tricuspid valve to measure RVSP
- Parasternal short axis view at the level of the mid papillary muscles

- Apical 4 chamber view with and without color Doppler of the mitral and tricuspid valves
- Continuous wave Doppler of the tricuspid valve to measure RVSP
- RV focused view to assess RV function
- Apical 5 chamber view with and without color Doppler of the aortic valve

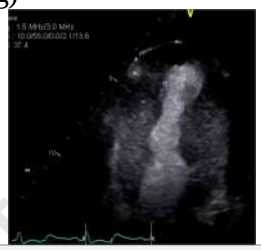
- Apical 2 and 3 chamber views with and without color Doppler of the mitral valve

- Subcostal view to assess LV and RV function.
- Subcostal view to measure IVC size and collapsibility with sniff

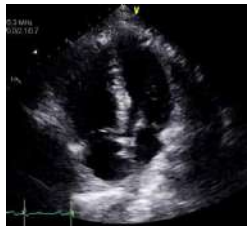
- Above protocol should be expanded in accordance with the presence of structural heart disease or to answer a specific clinical question.

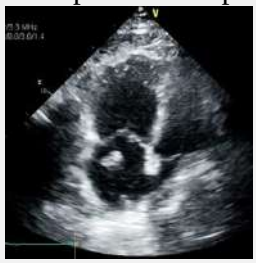
- All measurements should be performed off-line in order to minimize exposure to the operator during image acquisition.

Online Table 3: Summary of Imaging Findings from COVID-19 Associated Clinical Syndromes		
Imaging Modality	COVID-19 Associated Syndrome and Characteristic Findings	Examples

Echocardiography	• Takotsubo Cardiomyopathy
	  • Regional motion abnormalities typically with basal to midventricular hyperkinesis with akinesis/dykinesis of the apical LV segments. RV apex may also be involved
	  • Reverse pattern may also be seen with hyperkinesis of the apical segments
		Apical 2-chamber demonstrating hyperdynamic function, hypercontractility of the basal to midventricular LV segments and apical dyskinesis (ballooning)
		 

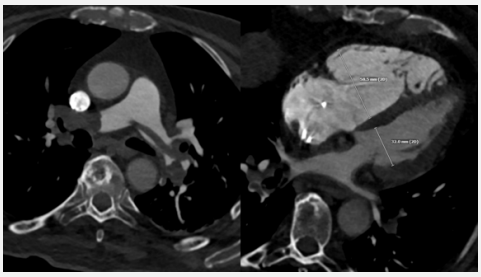
	• Asymptomatic LV dysfunction
	  • Global LV hypokinesis that may not follow regional coronary territories
	  • Typically, mild-moderate in severity	

	• Asymptomatic RV dysfunction (Pathway 1, Pathway 2, Pathway 3, Pathway 4) • RV enlargement with global hypokinesis can be seen in varying degrees with or without elevation in pulmonary pressures due to pulmonary involvement, magnitude of ventilatory support. In the setting of severe hypoxemia, regional dysfunction may also be seen similar to that seen in acute pulmonary embolism (see below).	Apical 4-chamber demonstrating RV enlargement 

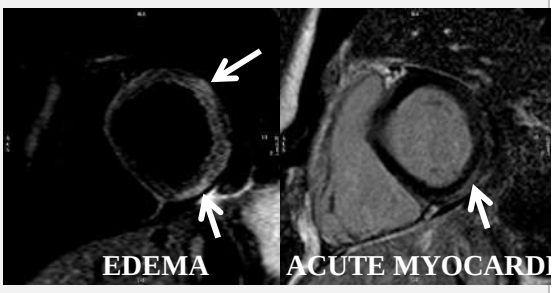
	• Acute Pulmonary Embolism with RV strain
	  • RV enlargement with associated hypokinesis
	  • May or may not have typical findings of acute RV strain “McConnell’s sign”: akinesis of the midventricular segment of the right ventricular free wall with relative preservation of apical contractility
	  • Supporting findings include worsened tricuspid regurgitation, elevated SPAP, visualized clot in transit
		Apical 4-chamber demonstrating RV enlargement with McConnell’s sign and thrombosis-in-situ traversing the right atrium and tricuspid annular plane
		 

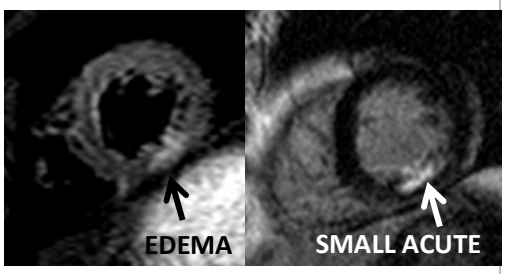
	• Acute Myocarditis • LV dysfunction can present in varying degrees from mild-moderate	

	to severe with hemodynamic instability. Abnormal global or regional strain may be seen in this setting	

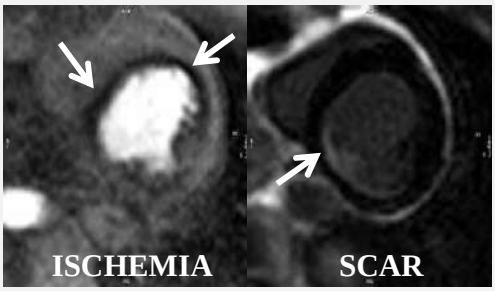
Chest CT
 	
CARDIAC CT
	• Acute Pulmonary Embolism
	  • Gold standard with high sensitivity and specificity, reproducibility, accuracy for diagnosis of acute main stem or subsegmental PE using high-resolution CT pulmonary angiography (PE protocol)
	  • Quantification and identification of embolic burden for use of anticoagulants versus thrombolytics
	  • Identification of degree of pulmonary artery obstruction and associated RV dysfunction
	  • RV/LV diameter index may be disproportionate due to interventricular septum leftward shift due to RV pressure overload, LV compression causing systolic dysfunction from underfilling, hemodynamic instability
		Contrast-enhanced chest CT showing central pulmonary embolism (left) with associated RV cavity dilatation (right).
		
		 

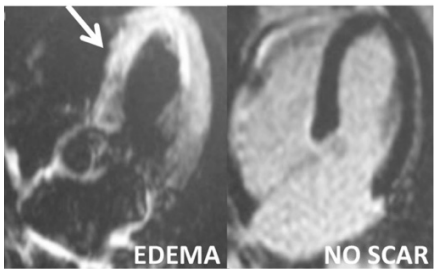
	• Coronary Embolism
	  • Direct embolism may result from thrombus originating from left-sided cardiac chambers, aortic/mitral endocarditis or thrombus, rarely cardiac tumors versus paradoxical embolism from venous system traversing through patent foramen ovale or atrial septal defect
	  • Filling defect seen in multiple coronary vascular territories, abrupt cut-off of coronary vessel in the absence of significant atherosclerosis
	  • Evidence of thrombosis in cardiac chambers (left atrial appendage, LV cavity)
	  • Assessment of myocardium may reveal perfusion defect due to myocardial injury.	

Cardiac MRI	• Acute Myocarditis
	  • Normal LV function or LV dysfunction in varying degrees from mild-moderate to severe with hemodynamic instability. CMR can provide biventricular functional analysis – location, degree, quantification, morphologic abnormalities
	  • May be associated with pericardial effusion
	  • Tissue characterization of quantity and location of edema (regional versus global) using T2-weighted imaging.
	  • Early gadolinium enhancement may be seen in acute tissue inflammation representing hyperemia and capillary leak
	  • Lake Louise Criteria may be helpful
	  • Late gadolinium enhancement may be seen representing either myocardial inflammation and/ or tissue necrosis / irreversible myocardial injury and fibrotic remodeling
		T2-weighted and post-contrast T1 weighted images of the LV short axis with evidence of myocardial inflammation and edema, and epicardial late enhancement in a patient with acute myocarditis.
		 

	• Myocardial Infarction
	  • May present as NSTEMI or STEMI with or without LV dysfunction – cine imaging can provide information on cardiac function, volume, mass, morphology, presence of pericardial effusion
	  • Global or regional wall motion abnormalities
	  • Rest/stress perfusion imaging can be used to detect ischemia, post MI risk stratification, quantification of myocardial blood flow reserve
	  • Allows for assessment of myocardial viability
	  • Tissue edema can be detected in the setting of ischemia and inflammation – regional edema that follows epicardial coronary distribution may suggest obstructive CAD as etiology versus patchy edema seen in MINOCA or myocarditis (see above)
	  • Late gadolinium enhancement can indicate myocardial scar from prior
		T2-weighted and post-contrast T1 weighted images of the LV short axis with evidence of focal transmural infarction and peri-infarct edema in a patient with acute myocardial infarction.
		 

	ischemia or fibrosis from prior inflammation; identification of small infarctions (embolic or spontaneous recanalization)	

	• Acute Myocardial Ischemia / Injury
	  • Allows for stress imaging for the assessment of suspected or known coronary artery disease
	  • Can also distinguish microvascular from macrovascular (epicardial) coronary disease by calculation of absolute myocardial blood flow (MBF)
	  • Allows for assessment of myocardial viability by identifying scarred myocardium
		Stress and post-contrast images of the LV short axis with evidence of subendocardial late gadolinium enhancement in the inferior wall suggestive of infarction (RCA territory) and inducible myocardial ischemia in the septum and anterior wall (LAD territory).
		 

	• Takotsubo Cardiomyopathy
	  • Regional motion abnormalities typically with basal to midventricular hyperkinesis with akinesia of the apical LV segments
	  • Reverse pattern may also be seen with hyperkinesis of the apical segments
	  • Diffuse transmural myocardial edema, corresponding to the areas of wall motion abnormalities
	  • Early gadolinium enhancement may be seen in acute tissue inflammation representing hyperemia and capillary leak
	  • No late gadolinium enhancement present (no scarring)
		T2-weighted and post-contrast T1 weighted images of the 4-chamber with evidence of extensive transmural edema and absence of infarction (in the presence of apical akinesia and ballooning).
		 

Cardiac PET / SPECT	• Myocardial Ischemia / Injury
	  • Allows for stress imaging for the assessment of suspected or known coronary artery disease
	  • Can also distinguish microvascular from macrovascular (epicardial) coronary disease by calculation of absolute myocardial blood flow	

	(MBF) and coronary flow reserve (CFR) • Allows for assessment of myocardial viability by quantification of coronary flow reserve to distinguish hibernating versus scarred myocardium	

	• Myocardial Inflammation / Myocarditis
	  • Pathologic myocardial FDG uptake suggestive of myocardial inflammation, myocardial hyperemia in the acute phase
	  • Chronic myocarditis patients may have inconclusive CMR findings of LGE – FDG-PET update can improve the specificity of CMR
		Rest perfusion and FDG PET scan showing focally increased glucose uptake, reflecting active inflammation.