Coronavirus disease 2019 (COVID-19): Myocardial injury

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INTRODUCTION

The coronavirus disease of 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously referred to as 2019-nCoV). Patients with COVID-19 commonly present with signs of myocardial injury. This topic will discuss evaluation and management of these patients.

Other cardiac issues in patients with COVID-19 are discussed separately:

- (See "Coronavirus disease 2019 (COVID-19): Coronary artery disease issues".)
- (See "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease".)

Other clinical aspects of COVID-19 are discussed separately:

- (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention".)
- (See "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension".)
- (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults".)
- (See "Coronavirus disease 2019 (COVID-19): Critical care issues".)
- (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability".)
- (See "Coronavirus disease 2019 (COVID-19): Outpatient management in adults".)
- (See "Coronavirus disease 2019 (COVID-19): Considerations in children".)
- (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

- (See "Coronavirus disease 2019 (COVID-19): Questions and answers".)

DEFINITION AND ETIOLOGY

The term "myocardial injury" encompasses all conditions causing cardiomyocyte death. Myocardial injury is commonly clinically identified by the presence of at least one cardiac troponin value above the 99th percentile upper reference limit (URL), in accordance with the Fourth Universal Definition of Myocardial Infarction [1]. High-sensitivity cardiac troponin levels are sensitive markers of myocardial injury; however, some patients with disease processes causing cardiomyocyte death may have troponin levels below the 99th percentile URL.

Cardiac troponin elevation does not distinguish among the causes of myocardial injury. Putative causes of myocardial injury in patients with COVID-19 include myocarditis (which may have a pseudo-infarct presentation with normal coronary arteries) [2,3], hypoxic injury, stress cardiomyopathy, ischemic injury caused by cardiac microvascular damage or epicardial coronary artery disease (with plaque rupture or demand ischemia), and systemic inflammatory response syndrome (cytokine storm) [4,5]. However, the contribution of each of these putative causes to myocardial injury in this setting has not been determined. It is also unknown whether angiotensin-converting-enzyme-2-related signaling pathways have a role in COVID-19-related cardiac injury. (See "Troponin testing: Clinical use" and "Elevated cardiac troponin concentration in the absence of an acute coronary syndrome" and "Diagnosis of acute myocardial infarction".)

Although some COVID-19 case reports have described findings consistent with a diagnosis of "clinically suspected myocarditis" [3] or possible stress cardiomyopathy [6-11], no case of biopsy- or autopsy-proven viral myocarditis caused by SARS-CoV-2 has been reported thus far. A case report described a patient with COVID-19 with regional wall motion abnormalities and endomyocardial biopsy findings consistent with lymphocytic myocarditis, but molecular analysis showed absence of SARS-CoV-2 genome in the myocardium [12]. A separate case report described a patient with COVID-19 who developed cardiogenic shock; light and electron microscopy of endomyocardial biopsy specimens revealed low-grade interstitial and endocardial inflammation, with viral particles identified in cytopathic macrophages but not in cardiomyocytes, which showed nonspecific features (eg, focal myofibrillar lysis and lipid droplets) [10]. These cases illustrate that identification of SARS-CoV-2 in specimens from the upper or lower respiratory tract is not sufficient to prove that myocardial injury was caused by SARS-CoV-2 myocarditis [6-8]. SARS-CoV-2 is not a known cardiotropic virus, and cardiotropic viruses that are known to be associated with myocarditis (eg, enterovirus, which is associated with diarrhea and parvovirus B19, which is associated with a pseudoinfarct presentation) were not searched for in most of the reported cases and might be involved. Proof that COVID-19 may be a new cause of viral myocarditis requires the presence of histological findings of active myocarditis

(ie, inflammatory lymphomonocytic infiltrates plus myocyte necrosis not typical of ischemic injury) plus the identification of the COVID-19 genome in heart tissue and/or identification of viral particles in cardiomyocytes in the absence of known cardiotropic viruses [3].

Limited data are available on autopsy findings in patients dying from COVID-19. In case reports describing autopsy results for six patients who died from COVID-19 (one patient in Beijing [13], two in Oklahoma [14], three in New Orleans [15]), histologic examination of cardiac tissue did not show myocarditic changes. Troponin levels were not reported for three of these patients; two of the three New Orleans cases had elevated antemortem troponin levels (up to twice the upper reference limit), and one case had troponin levels within the reference range. In the New Orleans case series, all of the patients had cardiovascular risk factors including hypertension, obesity, and gross examination revealed cardiomegaly and right ventricular dilation with no significant coronary artery stenosis or acute thrombus [15]. Histologic examination revealed scattered individual cardiomyocyte cell necrosis with no confluent areas of myocyte necrosis and rare areas with lymphocytes adjacent to but not surrounding degenerating myocytes. No viral cytopathic effect was identified by light microscopy, but studies for viral genome were not performed in this case series.

Further investigation, including histologic examination of cardiac tissue in COVID-19 patients, is required to characterize the relationship between COVID-19 and myocardial injury. Since biopsy-proven myocarditis may occur in the absence of troponin release, autopsy studies of COVID-19 victims, regardless of troponin levels, would be helpful in clarifying whether or not SARS-CoV-2 is a new cause of viral myocarditis.

PREVALENCE

Evidence of myocardial injury is common among patients hospitalized with COVID-19, but the causes of myocardial injury have not been elucidated, and its contribution to incident heart failure has not been well characterized.

Myocardial injury — The frequency of myocardial injury (as reflected by elevation in cardiac troponin levels) is variable among hospitalized patients with COVID-19, with reported frequencies of 7 to 28 percent [2,16-18]. Some studies have identified greater frequency and magnitude of troponin elevations in hospitalized patients with more severe disease and worse outcomes [2,16,19-21]. Data are lacking on the frequency of troponin elevations in asymptomatic or only mildly symptomatic patients with SARS-CoV-2 infection.

In a series of 416 patients with COVID-19 who were hospitalized in Wuhan, China, 19.7 percent had high-sensitivity troponin I (hs-TnI) above the 99th percentile upper reference limit on admission [2]. Patients with this marker of myocardial injury were older and had more comorbidities (including

chronic heart failure in 14.6 versus 1.5 percent), greater laboratory abnormalities (including higher levels of C-reactive protein, procalcitonin, and aspartate aminotransferase), more lung radiographic abnormalities, and more complications compared with those without myocardial injury. The mortality rate was also higher in those with myocardial injury (51.2 versus 4.5 percent). The risk of death starting from the time of symptom onset was more than four times higher in patients with evidence of myocardial injury on admission (hazard ratio 4.26; 95% CI 1.92-9.49).

In another study from Wuhan, elevation in hs-TnI above the 99th percentile upper reference limit was identified on admission in 46 percent of nonsurvivors versus 1 percent of survivors [20]. In contrast, a study of 24 critically ill COVID-19 patients in Seattle, with a 50 percent mortality rate, found elevated troponin levels early after intensive care unit admission in only 2 of 13 (15 percent) tested patients [18]. Some of the differences in frequency of troponin elevation may be due to use of differing troponin assays and differences in patient populations. Of note, only one study assessed and found considerably greater prevalence of preexisting cardiovascular disease and cardiac risk factors in patients with evidence of myocardial injury compared with those without elevated biomarkers [2]. Thus, it is not yet possible to determine whether myocardial injury is an independent risk marker in COVID-19 or if the risk associated with it is related to the burden of preexisting cardiovascular disease.

Heart failure — Limited data are available on the incidence of heart failure in patients with COVID-19. In a retrospective study of 799 patients hospitalized with COVID-19 in Wuhan, heart failure was identified as a complication in 49 percent of patients who died and in 3 percent of patients who recovered, despite a less than one percent baseline prevalence of chronic heart failure in the combined groups [22]. In a study of 191 patients hospitalized in two other medical centers in Wuhan, heart failure was identified in 52 percent of patients who died and in 12 percent of patients who recovered [20].

Although the acute heart failure incidence was not documented in some series of hospitalized patients with COVID-19, elevated natriuretic peptides (such as brain natriuretic peptide [BNP] and N-terminal proBNP [NT-proBNP]) have been identified, particularly in patients with evidence of cardiac injury. In the above described series of 416 hospitalized patients, NT-proBNP levels were significantly higher in patients with elevated troponin levels than in patients without troponin elevation (1689 versus 139 pg/mL) [2]. (See 'Myocardial injury' above.)

Heart failure in patients with COVID-19 may be precipitated by acute illness in patients with pre-existing known or undiagnosed heart disease (eg, coronary artery disease or hypertensive heart disease) or incident acute myocardial injury (eg, acute myocardial infarction, stress cardiomyopathy, cytokine storm, and other possible etiologies described above). Cardiovascular risk factors and cardiovascular disease are highly prevalent in hospitalized patients with COVID-19. For example, in a

report of 191 hospitalized patients in Wuhan, comorbidities included hypertension in 30 percent, diabetes mellitus in 19 percent, and coronary heart disease in 8 percent [20]. Patients with a known history of heart failure may suffer an acute decompensation due to the development of COVID-19 disease [9].

CLINICAL FEATURES

Clinical presentation — Most patients with COVID-19 with evidence of myocardial injury present with the typical symptoms and signs of SARS-CoV-2 infection such as fever, cough, dyspnea, and bilateral infiltrates on chest imaging, as described separately. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical manifestations'.)

A minority of patients with COVID-19 with evidence of myocardial injury present with cardiac symptoms (such as chest pain or palpitations [23]) or more nonspecific symptoms (fatigue); these symptoms may or may not be accompanied by prior or concurrent symptoms of respiratory infection [4,24].

Initial tests

Laboratory tests — Routine laboratory tests include a complete blood count with differential, serum electrolytes, blood urea nitrogen, creatinine, liver function tests, and blood glucose. (See "Evaluation of the patient with suspected heart failure", section on 'Initial panels'.)

ECG — A baseline electrocardiogram (ECG) is generally performed in patients presenting for acute care with suspected symptomatic COVID-19. This enables documentation of baseline QRS-T morphology should the patient develop symptoms or signs of a type of myocardial injury such as an acute coronary syndrome. Additionally, the baseline ECG allows for documentation of the QT (and corrected QTc) interval. Importantly, QTc will need to be monitored if QT-prolonging therapies are initiated (eg, azithromycin, chloroquine) to reduce the risk of acquired long QT syndrome. (See "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease", section on 'ECG' and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease", section on 'Patients receiving QT-prolonging treatments (eg, hydroxychloroquine, chloroquine, azithromycin, etc)' and "Acquired long QT syndrome: Clinical manifestations, diagnosis, and management".)

ECG abnormalities that have been reported in patients with COVID-19 and troponin elevation include T-wave depression and inversion, ST-segment depression, and Q waves [2]. ST-segment elevation

has been reported in patients with findings consistent with clinically suspected myocarditis or stress cardiomyopathy [6,8].

The most common arrhythmia in patients with COVID-19 is sinus tachycardia but atrial fibrillation, atrial flutter, or ventricular tachycardia may occur. (See "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease".)

Troponin — Troponin testing is commonly performed in hospitalized patients with COVID-19, as it may have prognostic value and may serve as a useful baseline for comparison in patients who develop manifestations of possible myocardial injury (such as heart failure or arrhythmia). Some experts also perform troponin testing in selected outpatients with uncertain level of risk. As mentioned above, among patients with COVID-19, troponin levels are most prevalent and most elevated with more severe disease [17,25]. An elevated troponin is likely not indicative of an acute coronary syndrome in the absence of suggestive symptoms, signs, or ECG findings.

In patients with COVID-19, troponin elevation may be initially detected prior to, at the time of, or following hospital admission [6-9,17,20,21,26]. A variety of time courses for troponin elevation have been observed:

- **Mild** – Patients hospitalized with COVID-19 commonly have mild troponin elevation (typically <99th percentile upper reference limit), with modest rise or fall on subsequent days, typically remaining well below the 99th percentile upper reference limit [17]. This appears to be the most common pattern of troponin elevation in patients with COVID-19 and is often associated with no cardiac symptoms. This pattern has been described in patients with COVID-19 who survived after hospitalization [20].

- **Moderate time-limited** – Early moderate troponin elevation (which may approach or exceed the 99th percentile upper reference limit), which may fall on subsequent days. This pattern was seen in anecdotal reports of patients with clinically suspected myocarditis or stress cardiomyopathy [6-9].

- **Progressive** – Some patients with moderate troponin elevation at hospital admission suffer clinical deterioration with respiratory failure accompanied by progressive troponin elevation, along with elevations in other biomarkers (eg, D-dimer, interleukin-6, ferritin, and lactate dehydrogenase) with accelerated rise after the second week of hospitalization [20,21]. This progression to cytokine storm has been described in nonsurvivors, with death occurring at a median of 18.5 days after symptom onset [20].

Natriuretic peptide — A natriuretic peptide level (B-type natriuretic peptide [BNP] or N-terminal proBNP) is obtained in patients with suspected heart failure if the diagnosis of heart failure is

uncertain. (See "Evaluation of the patient with suspected heart failure", section on 'BNP and NT-proBNP'.)

As described above, natriuretic peptide levels are commonly elevated in hospitalized patients with COVID-19, particularly in patients with elevated cardiac troponin levels. (See 'Heart failure' above.)

DIAGNOSIS

When to suspect myocardial injury and key considerations — Myocardial injury should be suspected in patients with COVID-19 with one or more of the following new findings: troponin elevation, global or regional left ventricular wall motion abnormalities, unexplained cardiac arrhythmias, or ECG changes (particularly diffuse ST elevation).

Diagnostic evaluation

Key considerations — The approach to evaluation of myocardial injury in patients with known or suspected COVID-19 may differ from the standard approach to evaluation of myocarditis, as it is based upon weighing the following considerations [25]:

- The likelihood that evaluation will change management. Thus, it is important to identify a treatable cause of myocardial injury that requires timely intervention, such as acute myocardial infarction.
- Considerations of nosocomial infection control to limit the spread of disease.
- Optimal management of limited available medical staff and resources to provide for the health care needs of the community.

Diagnostic approach — The diagnostic evaluation includes the following components (see "Clinical manifestations and diagnosis of myocarditis in adults", section on 'Approach to diagnosis of myocarditis'):

- Clinical evaluation includes history, physical examination, ECG, serum cardiac troponin levels, and initial laboratory tests to assess for symptoms and signs of heart failure and possible causes (including conditions unrelated to SARS-CoV-2 infection). Natriuretic peptide (B-type natriuretic peptide [BNP] or N-terminal proBNP) measurement is indicated if the diagnosis of heart failure is uncertain. (See 'Initial tests' above.)
- Decisions regarding the need for further evaluation are based upon whether test results will alter clinical management.

- If the clinical presentation is suggestive of acute coronary syndrome (ACS), timely evaluation is required to determine if urgent intervention is indicated. There is an elevated risk of ACS among patients with COVID-19 given the high prevalence of comorbidities in this patient population. Evaluation of coronary disease in patients with COVID-19 is discussed separately. (See "Coronavirus disease 2019 (COVID-19): Coronary artery disease issues".)

- For patients with COVID-19 without suspected ACS:

  - Most patients with mild troponin elevation without symptoms and signs of acute heart failure can be clinically monitored without cardiac imaging.

  - For patients who develop new onset heart failure, echocardiogram may be performed to evaluate regional and global ventricular and valvular function if this is requested by a consulting cardiologist and is expected to have a significant impact on management or is likely to change the patient's prognosis. Echocardiography findings that have been described in case reports of patients with COVID-19 include focal and global left ventricular wall motion abnormalities and pericardial effusion.

- For patients with a ventricular motion abnormality, elevated troponin, and no ACS, possible diagnoses include stress cardiomyopathy and clinically suspected myocarditis (along with other causes of myocardial injury described above). (See 'Myocardial injury' above.)

  - A diagnosis of stress cardiomyopathy is based on identification of the following four features: transient left ventricular systolic dysfunction (typically not in a single coronary distribution; patterns include apical, mid-ventricular, and basal), absence of angiographic evidence of obstructive coronary disease or acute plaque rupture; presence of new ECG abnormalities (either ST-segment elevation and/or T-wave inversion); **or** modest elevation in cardiac troponin and absence of pheochromocytoma or myocarditis. The diagnostic evaluation of stress cardiomyopathy is discussed separately. (See "Clinical manifestations and diagnosis of stress (takotsubo) cardiomyopathy".)

  - In patients with COVID-19 with suspected myocarditis, the decision on whether to proceed with further evaluation for myocarditis (with cardiovascular magnetic resonance imaging [CMR] and possible endomyocardial biopsy) is based on the likelihood of a diagnosis that would alter therapy. Care must be taken to balance the risk of potential nosocomial spread of the disease and benefit of this additional information to modifying treatment. (See "Clinical manifestations and diagnosis of myocarditis in adults", section on 'Diagnosis'.)

    - Since there is no established therapy for clinically suspected myocarditis, we do not recommend routine evaluation for myocarditis in patients with COVID-19. Although case

reports have described empiric immunotherapy in a few patients with COVID-19 with clinically suspected myocarditis (with or without CMR confirmation), the safety and efficacy of such therapy are uncertain.

- Evaluation for myocarditis by endomyocardial biopsy (with or without prior CMR, depending on the patient's condition and available resources) may be appropriate in selected cases when a treatable type of myocarditis is suspected (eg, giant cell myocarditis), or in the presence of severe unexplained biventricular dysfunction, unexplained cardiogenic shock, or unexplained life-threatening arrhythmia with normal coronary arteries (with or without troponin increase) to confirm a definitive diagnosis of myocarditis and identify its cause to enable possible etiology-directed therapy [3]. Since biopsy-proven myocarditis is highly prevalent in young patients and very rare in the elderly, the clinical suspicion of myocarditis should be higher, and the threshold to perform an endomyocardial biopsy should be lower in young patients without cardiovascular comorbidities. (See "Clinical manifestations and diagnosis of myocarditis in adults", section on 'Approach to diagnosis of myocarditis' and "Treatment and prognosis of myocarditis in adults", section on 'Management of specific disorders'.)

MANAGEMENT

General approach

Supportive cardiac care — The optimal management for myocardial injury associated with COVID-19 has not been determined. Thus, the management of patients with myocardial injury, including clinically suspected myocarditis, involves supportive care (including management of heart failure, therapy for arrhythmias, and avoidance of cardiotoxins), as discussed separately. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults" and "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension" and "Coronavirus disease 2019 (COVID-19): Critical care issues" and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease", section on 'Management' and "Treatment and prognosis of myocarditis in adults", section on 'General management' and "Treatment of acute decompensated heart failure: General considerations" and "Treatment of acute decompensated heart failure: Components of therapy" and "Overview of the management of heart failure with reduced ejection fraction in adults" and "Treatment and prognosis of heart failure with preserved ejection fraction" and "Treatment and prognosis of heart failure with mid-range ejection fraction".)

Patients with COVID-19 and heart failure or asymptomatic left ventricular systolic dysfunction should receive standard therapy for these conditions including pharmacologic therapy, careful management

of fluid balance, and advanced therapies as needed. (See "Treatment of acute decompensated heart failure: General considerations" and "Treatment of acute decompensated heart failure: Components of therapy" and "Overview of the management of heart failure with reduced ejection fraction in adults" and "Treatment and prognosis of heart failure with preserved ejection fraction" and "Management of refractory heart failure with reduced ejection fraction" and "Management and prognosis of asymptomatic left ventricular systolic dysfunction".)

General management including thromboprophylaxis — General management of COVID-19 and critical care issues are discussed separately. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults" and "Coronavirus disease 2019 (COVID-19): Critical care issues".)

Hypercoagulability and the role of thromboprophylaxis in patients with COVID-19 are discussed separately. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability".)

Investigational — While laboratory evidence of a marked inflammatory response, similar to cytokine release syndrome, is associated with critical and fatal illness in patients with COVID-19, no treatment has been identified for this syndrome. Investigational protocols using the interleukin 6 inhibitors tocilizumab and sarilumab are ongoing. (See "Treatment and prognosis of myocarditis in adults", section on 'Management of specific disorders' and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention".)

ACE inhibitors and ARBs — Of note, standard indications for an angiotensin receptor-neprilysin inhibitor, angiotensin converting enzyme (ACE) inhibitor, or angiotensin receptor blocker (ARB) in treatment of heart failure with reduced ejection fraction (and for the latter two drugs in treatment of hypertension) apply to patients with COVID-19. Although there has been speculation that elevated ACE2 levels caused by renin-angiotensin-aldosterone system inhibitors might impact susceptibility to SARS-CoV-2 because ACE2 is a receptor for this virus, there is no evidence that treatment with these drugs worsens the clinical course of SARS-CoV-2 infection. (See "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension", section on 'Renin angiotensin system inhibitors'.)

Issues for ventricular assist devices and cardiac transplantation — Patients supported by left ventricular assist devices (LVADs) may present with low-flow alarms due to the vasodilation coupled with diarrhea and dehydration, which can occur with COVID-19 infection. However, vigorous fluid resuscitation can result in right heart failure in these LVAD patients. (See "Practical management of long-term mechanical circulatory support devices", section on 'Right heart failure' and "Right heart failure: Causes and management".)

Whether maintenance immunosuppression for cardiac transplant recipients should be altered and whether these patients have more or less severe COVID-19 is unknown. There has been some suggestion that the late stage of COVID-19 associated with acute respiratory distress syndrome may be alleviated by the presence of immunosuppression, as it may reduce the cytokine response. Many heart transplant centers have reduced antiproliferative agents (eg, mycophenolate mofetil) in patients with COVID-19 infection [9,17]; generally, calcineurin inhibitors and prednisone doses have been maintained in this setting. (See "Heart transplantation in adults: Induction and maintenance of immunosuppressive therapy".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Coronavirus disease 2019 (COVID-19) – International and government guidelines for general care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Guidelines for specialty care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Resources for patients".)

SUMMARY AND RECOMMENDATIONS

- The term "myocardial injury" encompasses all conditions causing cardiomyocyte death. Myocardial injury is commonly clinically identified by the presence of at least one cardiac troponin value above the 99th percentile upper reference limit (URL). High-sensitivity cardiac troponin levels are sensitive markers of myocardial injury; however, some patients with disease processes causing cardiomyocyte death may have troponin levels below the 99th percentile URL. (See 'Definition and etiology' above.)

- Putative causes of myocardial injury in patients with COVID-19 include myocarditis, hypoxic injury, stress cardiomyopathy, ischemic injury caused by cardiac microvascular damage or epicardial coronary artery disease (with plaque rupture or demand ischemia), and systemic inflammatory response syndrome (cytokine storm). However, the contribution of each of these putative causes to myocardial injury in this setting has not been determined. Thus far, no case of biopsy- or autopsy-proven viral myocarditis caused by COVID-19 has been reported; further investigation, including histologic examination of cardiac tissue from COVID-19 patients with the identification of findings of active myocarditis plus COVID-19 genome in heart tissue and/or identification of viral particles in cardiomyocytes in the absence of known cardiotropic viruses, is required to prove that COVID-19 is a novel cause of viral myocarditis. (See 'Definition and etiology' above.)

- Myocardial injury (as reflected in elevated cardiac troponin levels) is common among patients hospitalized with COVID-19, but the causes of myocardial injury have not been elucidated, and its contribution to incident heart failure has not been well characterized. Greater frequency and magnitude of troponin elevations are associated with more severe disease and worse outcomes. (See 'Myocardial injury' above.)

- Incident heart failure may be common in hospitalized patients with COVID-19. Heart failure in patients with COVID-19 may be precipitated by acute illness in patients with preexisting known or undiagnosed heart disease (eg, coronary artery disease or hypertensive heart disease) or incident acute myocardial injury (eg, acute myocardial infarction, stress cardiomyopathy, and other possible etiologies described above). (See 'Heart failure' above.)

- Most patients with COVID-19 with evidence of myocardial injury present with the typical symptoms and signs of SARS-CoV-2 infection such as fever, cough, dyspnea, and bilateral infiltrates on chest imaging. A minority of patients with COVID-19 with evidence of myocardial injury present with cardiac symptoms (such as chest pain or palpitations). (See 'Clinical presentation' above and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical manifestations'.)

- Patterns of troponin elevation in hospitalized patients with COVID-19 include mild limited elevation (the most common pattern), a moderate time-limited elevation (which may approach or exceed the 99th percentile upper reference limit), and a progressive pattern with moderate elevation followed by a progressive elevation along with rise of other biomarkers consistent with cytokine storm. (See 'Troponin' above.)

- If the clinical presentation is suggestive of acute coronary syndrome (ACS), timely evaluation is required to determine if urgent intervention is indicated. Evaluation of coronary disease in patients with COVID-19 is discussed separately. (See 'Diagnosis' above and "Coronavirus disease 2019 (COVID-19): Coronary artery disease issues".)

- Most patients with COVID-19 without suspected ACS, with mild troponin elevation, and without acute heart failure can be clinically monitored without cardiac imaging. For patients who develop new onset heart failure, echocardiogram may be performed to evaluate regional and global ventricular and valvular function if this is requested by a consulting cardiologist and is expected to have a significant impact on management or is likely to change the patient's prognosis. (See 'Diagnosis' above.)

- Since there is no established therapy for clinically suspected myocarditis, we do not recommend routine evaluation for myocarditis in patients with COVID-19. Evaluation for myocarditis by endomyocardial biopsy (with or without prior cardiac magnetic resonance imaging, depending on

the patient's condition and available resources) may be appropriate in selected cases when a treatable type of myocarditis is suspected (eg, giant cell myocarditis) or in the presence of severe unexplained biventricular dysfunction, unexplained cardiogenic shock, or unexplained life-threatening arrhythmia with normal coronary arteries (with or without troponin increase) to confirm a definitive diagnosis of myocarditis and identify its cause to enable possible etiology-directed therapy. Since biopsy-proven myocarditis is highly prevalent in young patients and very rare in the elderly, the clinical suspicion of myocarditis should be higher, and the threshold to perform an endomyocardial biopsy should be lower in young patients without cardiovascular comorbidities. (See 'Diagnostic evaluation' above and "Clinical manifestations and diagnosis of myocarditis in adults", section on 'Diagnosis'.)

- The optimal management for myocardial injury associated with COVID-19 has not been determined. Thus, the management of patients with myocardial injury, including clinically suspected myocarditis (with or without cardiovascular magnetic resonance confirmation), involves supportive care (including management of heart failure, therapy for arrhythmias and avoidance of cardiotoxins), as discussed separately. (See 'Management' above and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease", section on 'Management' and "Treatment and prognosis of myocarditis in adults", section on 'General management' and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease".)

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Contributor Disclosures

Alida LP Caforio, MD, PhD, FESC Nothing to disclose **Donna Mancini, MD** Grant/Research/Clinical Trial Support: Shire [ADHD (Guanfacine)]. Consultant/Advisory Boards: AstraZeneca [Dyslipidaemia (Rosuvastatin)]. Consultant/Advisory Boards: United Therapeutics [DSMB]. **Susan B Yeon, MD, JD, FACC** Nothing to disclose

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