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CLINICAL GUIDANCE—CME

PM&R

Multi-disciplinary collaborative consensus guidance statement on the assessment and treatment of cardiovascular complications in patients with post-acute sequelae of SARS-CoV-2 infection (PASC)

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19), has caused substantial mortality and morbidity worldwide since late 2019. The postacute sequelae of SARS-CoV-2 infection (PASC) can manifest as a wide range of new, recurring, or ongoing disabling symptoms or health problems that people can experience from the time of acute infection and persisting or starting 4 or more weeks after being infected with the virus that causes COVID-19.

More than 100 symptoms have been reported with PASC.[1] The more common symptoms include fatigue, shortness of breath, chest discomfort/pains, palpitations, cognitive dysfunction (“brain fog”), sleep disorders, fevers, gastrointestinal symptoms, anxiety, and depression.[1] It is important to recognize that individuals who did not have acute COVID-19 symptoms in the days or weeks after they were infected can develop PASC symptoms and conditions weeks to months after acute infection. These post-COVID conditions have also been reported using the terms long COVID, long-haul COVID, post-acute COVID-19, long-term effects of COVID, or chronic COVID.[2] This guidance statement uses the terminology PASC and focuses on the assessment and treatment of cardiovascular complications of PASC.

Growing evidence indicates that COVID-19 related cardiovascular symptoms and complications may arise or persist weeks or months after resolution of the acute infection and can range from mild to incapacitating.[3] Among survivors of COVID-19, 5%–29% report chest pain, dyspnea, or palpitations post recovery, even 6 months after the acute infection.[4] Despite the prevalence of these sequelae and emerging data on longevity of symptoms, limited guidance exists regarding the assessment and treatment of cardiovascular complications in PASC. The American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary PASC Collaborative (PASC Collaborative) was convened to address the pressing need for guidance in the care of patients with PASC.

The incidence and trajectory of PASC in unvaccinated versus vaccinated patients with “breakthrough” cases (including but not limited to current and emerging variants of the virus) is evolving. The PASC Collaborative took this into account during the development process, and these guidance statements generally apply to individuals who develop PASC regardless of their vaccination status. In addition, it is acknowledged that systematic study is needed to develop an evidence-based approach to caring for patients with PASC. The goal of this and other statements is to provide practical guidance to clinicians in the assessment and treatment of individuals presenting with PASC.

PASC CONSENSUS GUIDANCE STATEMENT METHODS

The AAPM&R PASC Collaborative is developing expert recommendations and guidance from established PASC centers with experience in managing individuals with PASC. The PASC Collaborative is following an iterative, modified Delphi process to achieve consensus on assessment and treatment recommendations for a series of Consensus Guidance Statements focused on the most prominent PASC symptoms. There is an intentional focus on health equity as disparities in care and outcomes are critically important to address. Beyond patient care, the hope is that a broadened understanding of current patient care practices will help identify areas of future research. A full description of the methodology has been published in a previous issue.[5]

We acknowledge that the definition of PASC is evolving, and there are various factors that contribute to diagnosis and management. Literature available at the time of our consensus process suggested that PASC be defined as the persistence of symptoms beyond 3 or 4 weeks from the onset of acute infection.[6] Alternative definitions of PASC include symptoms lasting longer than 3 months.[7] Following the completion of our consensus process for this report, the World Health Organization released a definition of “post-COVID condition,” including describing the timing as “usually 3 months from the onset of COVID-19” and lasting “for at least 2 months.”[8] Based on patient feedback during our consensus process, we agree that earlier evaluation, diagnosis, and management can improve access to beneficial interventions. For the purposes of this guidance statement, we recommend expanded assessment if symptoms are not improving 1 month after acute symptom onset.

These Consensus Guidance Statements are intended to reflect current practice in patient assessment, testing, and treatments. They should not preclude clinical judgment and must be applied in the context of the specific patient, with adjustments for patient preferences, comorbidities, and other factors.

EDUCATION OF INDIVIDUALS WITH PASC AND HEALTH CARE PROFESSIONALS

Education of health care professionals and individuals with PASC is central to successfully caring for individuals with PASC and should be based on current evidence and clinical experience.[9–11]

It is recommended that education include the following:

1. The Heterogeneity of PASC Symptoms: Although fatigue, headache, brain fog, and shortness of breath are reported most frequently, as referenced previously, up to 100 different symptoms have been reported by individuals with PASC.[1] Education should address the heterogeneity of cardiovascular symptoms associated with PASC and the waxing and waning nature of such symptoms.[12,13]
2. Likelihood of Developing PASC: PASC appears more likely to occur in patients with more severe initial infections and/or poorer baseline health. Gender and race/ethnicity disparities have also been reported, though this literature is evolving.[14]

3. Clinical Red Flags vs. Anticipated Symptoms: Individuals with PASC undergoing an initial evaluation should be educated on the signs and symptoms consistent with PASC and the non-life-threatening nature of these symptoms. Clinicians should discuss the differentiation of cardiovascular "red flags" from the clinical presentation of PASC including the use of symptom visual analog scales (VAS), physiological data (blood pressure, heart rate), and clinically safe ranges for metrics consistent with PASC. An open dialogue facilitates understanding of the trends of anticipated symptoms.
4. Pacing and Energy Conservation: Energy conservation strategies are options to ameliorate symptom exacerbations including postexertional malaise (PEM) in PASC and many other chronic disease states, including myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).[15–17] PEM is the worsening of symptoms following even minor physical or mental exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks.[18] Pacing strategies include dividing daily tasks into smaller, manageable components to prevent symptom exacerbation. It differentiates tolerated tasks from symptom-exacerbating triggers to optimize activity tolerance.[19,20] Using symptom assessment with VAS and the Borg Rate of Perceived Exertion Scale (RPE) may assist patients in quantifying symptoms to better recognize symptom exacerbations.[21,22]
5. Understanding the Interrelationship of the Cardiovascular and Autonomic Nervous Systems: Individuals with PASC and health care professionals managing them should be educated on the interplay between the cardiovascular and autonomic nervous systems[23,24] and their role in regulation of heart rate, blood pressure, etc.[25] Education should include the etiology of symptoms, possible patterns of symptom evolution and exacerbation, and the recognition of "triggers" or exacerbating factors.[17,26,27]

CARDIOVASCULAR COMPLICATIONS IN PATIENTS WITH PASC

Acute COVID-19 may involve multiple organ systems.[28] The severity of involvement often corresponds to the severity of acute COVID-19[29] illness and need for hospitalization, intensive care (ICU), and supportive respiratory and cardiac interventions. Acute disease not requiring hospitalization may also be associated with multiple organ system involvement.[30]

Involvement of the cardiovascular system may include heart (myocardium, coronary vessels, conduction system), peripheral vasculature (venous thrombosis), central vasculature (cerebrovascular—stoke, and cardiopulmonary—pulmonary embolism), as well as the "central" neuro-hormonal/autonomic control of the cardiovascular system.[31] Individuals with preexisting heart disease and risk factors for heart disease are at increased risk of severe COVID-19 disease[32] and death, including from further cardiovascular system involvement.

In more severe and acute COVID-19 disease, reported cardiovascular disease includes myocardial infarction (MI), heart failure, dysrhythmias, myocarditis and pericarditis, venous thrombosis, and thromboembolic disease. In less severe and postacute COVID-19 disease, reported cardiovascular disease includes myocarditis, pericarditis, autonomic dysfunction, persistent dysrhythmias, heart failure, and late effects of venous thromboembolism.

In general, individuals with PASC-related cardiovascular disease may present with symptoms including shortness of breath, fatigue, chest pain, palpitations, dizziness, abdominal bloating, leg swelling, and impaired activity tolerance. In individuals with coexistent PASC-related autonomic dysfunction, related symptoms may significantly overlap with those of heart disease. Careful consideration and, at times, specific testing may be needed to differentiate cardiovascular disease from autonomic dysfunction, or to confirm the coexistence of both.

Symptom severity and impact can be highly variable between individuals with PASC as well as over time within the same individual. There is currently an incomplete understanding of the etiology of PASC and, at times, a lack of objective findings. For these reasons, we recommend clinicians following individuals with PASC maintain an open mind to the potential development of cardiovascular symptoms and disease through the course of PASC. It is also important to recognize that many individuals with PASC and complex symptomatology report their symptoms as being *minimized* by clinicians leading to a breakdown in the clinician–patient relationship. As such, individuals with PASC and PASC-related cardiovascular complications may be mis- or undiagnosed. Caution is also recommended when discussing mental health considerations such as anxiety, stress, and depression. Although the COVID-19 pandemic in general and PASC-related cardiovascular symptoms specifically can result in or exacerbate emotional disorders, focusing on a mental health cause of cardiovascular symptoms can undermine the trust in and partnering relationship the individual with PASC has with the clinician. Management of mental health disorders is an integral element of the management of cardiovascular complications in PASC and will be discussed in a forthcoming PASC Collaborative Guidance statement.

The reported incidence of cardiovascular complications due to acute COVID-19 disease[32] includes:

- Myocardial injury: 7%–40% (MI; transient myocardial ischemia; acute nonischemic myocardial injury) with

a higher prevalence among those requiring intensive care
- Acute heart failure: 23%–33% among hospitalized patients
- Right ventricular (RV) dysfunction: 16%–35%
- RV dilation: 12%–15%
- Arrhythmias: 18% (atrial fibrillation/flutter most common)
  - 4%–6% are life-threatening arrhythmias (ventricular tachycardia/ventricular fibrillation) and more common in those with elevated cardiac troponins
- Venous thromboembolism: 15%–21% in hospitalized patients[31]

In post-acute COVID, the incidence of pulmonary embolism, arterial and venous thromboses, MI, and stroke are all elevated.[33] Overall incidence of ischemic stroke and MI is reported to be nearly 4% across studies. Myocardial abnormalities on cardiac magnetic resonance (CMR) imaging have been noted in 78% of patients within 2–3 months of acute COVID-19, irrespective of severity of the initial infection.[34] Myocarditis—ongoing myocardial inflammation—was noted in up to 60% during this time period. Cardiac injury including MI, myocarditis, and heart failure is reported in 10%–52% of patients previously hospitalized for COVID-19.[35]

Predictive models have been used to estimate the incidence of long-term cardiovascular complications of COVID-19 indicating that the risk and 1-year burden of cardiovascular diseases in survivors of acute COVID-19 are substantial.[36] Beyond the first 30 days after infection, individuals with COVID-19 are at increased risk of cardiovascular disease including cerebrovascular disorders, dysrhythmias, ischemic and nonischemic heart disease, pericarditis, myocarditis, heart failure, and thromboembolic disease. The risk was evident even among individuals who were not hospitalized during acute COVID-19 infection and increased in a graded fashion according to the intensity of illness and required care setting during the acute illness—nonhospitalized, hospitalized, and admitted to intensive care. The risks were evident regardless of age, race, gender, and other cardiovascular risk factors, including obesity, hypertension, diabetes, chronic kidney disease, and hyperlipidemia; they were also evident in people without any cardiovascular disease before exposure to COVID-19, providing evidence that these risks might manifest even in people at low risk of cardiovascular disease.[36]

ASSESSMENT OF CARDIOVASCULAR COMPLICATIONS IN PASC

Attention to cardiovascular health and early identification and optimal management of cardiovascular risk factors and disease are essential for the longer-term health of individuals with PASC and for the broader perspective of the health of our nation. The risks and 12-month burden of cardiovascular diseases may translate into a significant number of potentially affected people globally. Governments and health systems around the world must be prepared to deal with the likely significant contribution of the COVID-19 pandemic to a rise in the burden of cardiovascular diseases. Because of the chronic nature of these conditions, they will likely have long-lasting consequences for patients and health systems and also have broad implications on economic productivity and life expectancy.[36]

As noted in the AAPM&R Multi-Disciplinary PASC Consensus Guidance Statement methodology,[5] the recommendations that follow (Table 1: Recommendations for the Assessment of Cardiovascular Complications in Patients with PASC) are based on expert consensus and are followed by additional discussion, when appropriate.

Discussion: Assessment of cardiovascular complications in individuals with PASC

Patient history

The initial evaluation of individuals with PASC with presumed cardiovascular symptoms includes a review of: relevant past medical history including risk factors for cardiovascular disease; the acute COVID-19 course—asymptomatic/mild/moderate/severe; events during relevant hospitalizations and location of management—home/hospital/ICU; need for ventilator, extra-corporeal membrane oxygenation (ECMO). Current cardiovascular history should differentiate cardiac symptoms (chest pain, palpitations), from those due to pulmonary, autonomic, neurologic or other systems. Atypical presentation of cardiovascular disease should be considered in the history: women with PASC and coronary artery disease (CAD) may present with dyspnea on exertion and "atypical" chest pain rather than central chest pressure on exertion; individuals with PASC and preexisting diabetes may have asymptomatic angina due to autonomic dysfunction; individuals with PASC and with preexisting, worsened, or new cognitive or communication disorders may not be able to accurately describe cardiovascular symptoms.

A review of current medications focusing on those prescribed for cardiovascular conditions and those with potential side effects that can impact the cardiovascular system is recommended. Medications commonly used in CV complications that can also affect the CV system include: Betablockers, calcium channel blockers, ACE inhibitors/ ARBs, diuretics, statins, mineralocorticoid receptor agonists and antagonists, anti-arrhythmic agents, anticoagulants, alpha 1 antagonists and

TABLE 1 Recommendations for the assessment of cardiovascular complications in patients with PASC

#	Cardiovascular complications assessment statement
1a	Patient History: A full patient history should be performed to include review of predisposing comorbidities, prior cardiovascular events, severity of the initial COVID-19 illness—mild, moderate, severe, including relevant hospitalization and care in the intensive care unit (ICU), need for ventilator, extra-corporeal membrane oxygenation (ECMO) etc., and timeline of symptom evolution. Additional components of the patient history should address: • Most common new or worsening cardiac symptoms: chest pain, palpitations, shortness of breath, near-or syncopal episodes, exercise intolerance, fatigue, • Studies conducted to date: labs, electrocardiogram, echocardiogram , chest imaging, other cardiac work-up if done (cardiac catheterization, cardiac magnetic resonance imaging, etc.), • Medication history—Evaluate for medications that may impact symptoms, signs or assessment parameters (ie, medications with anti-arrhythmic, diuretic or vaso-active impact).
1b	Patient History: Symptoms should be characterized to understand contributing factors that limit activity including onset (new, acute or chronic), frequency, intensity, aggravating and alleviating factors, etc.
2a	Initial Evaluation: Clinicians should conduct a thorough examination of the cardiovascular system including routine vital signs (heart rate [HR], blood pressure [BP], pulse oximetry), auscultation of heart and lungs, peripheral pulses and bruits, and signs of volume overload.
2b	Initial Evaluation: For individuals reporting dizziness, lightheadedness, and syncope/presyncope clinicians should further characterize the perceived dizziness (lightheadedness vs. room spinning sensation) and differentiate between central or peripheral etiologies which warrant specialist referral.
2c	Initial Evaluation: To differentiate cardiovascular from autonomic dysfunction, check for orthostatic blood pressure and heart rate response in supine and standing position. If abnormal or symptoms are concerning for autonomic dysfunction, continue evaluation as per the autonomic dysfunction guideline including a 10-min active stand test. (Blitshteyn S, Abramoff B, Azola A, et al. Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Autonomic Dysfunction in Patients with Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): submitted to *PM&R*, under review)
3	Order basic laboratory work-up in individuals with cardiac symptoms, or those without lab work-up in the 3 months prior to the visit. Consider: complete blood count, basic metabolic panel, troponin level (preferably high-sensitivity), brain natriuretic peptide or N-terminal pro b-type natriuretic peptide, D-dimer, C-reactive protein and erythrocyte sedimentation rate, lipid panel. Further laboratory work-up may be considered based on the results of the basic tests or if there is concern for specific cardiac conditions.
4	Clinicians should consider ordering electrocardiogram, echocardiogram, and/or ambulatory cardiac monitoring. • Holter for symptoms occurring every day. • 14-day monitor (e.g., Ziopatch) for symptoms occurring every few days • Event monitor (looping or non-looping, mobile cardiac telemetry) for infrequent symptoms.
5	Where diagnosis is uncertain or symptoms are progressing or severe consider referral to a cardiologist for more detailed assessment (computed tomography of the chest, cardiac magnetic resonance imaging, cardiac stress testing, cardiopulmonary exercise testing).
6	On initial evaluation, obtain standardized measures of activity performance to compare to normal control values and to guide the initial activity prescription. Repeat the standardized measures of activity performance at follow-up visits to quantify functional changes and guide progression of the activity prescription.

Abbreviation: PASC, postacute sequelae of SARS-CoV-2 infection.

agonists, ivabradine, anti-platelet agents, and QT prolonging medications. For a comprehensive review of medications specific for the cardiovascular system reference Chapter 17 of Pathophysiology of Heart Disease: Cardiovascular Drugs.[37] A review of over-the-counter (OTC) medications/herbs/supplements/vitamins is recommended to determine if they may be affecting symptoms. Of note, OTC nonsteroidal anti-inflammatory medications can cause salt and water retention worsening pedal edema and heart failure, alpha agonist cough/cold decongestant medications can cause tachycardia, antihistamines can cause QT prolongation and promote arrhythmias, and fish oil supplements can cause arrhythmias.[38,39]

A review of cardiovascular disease risk factors is recommended, including hypertension, dyslipidemia, dietary habits, obesity, diabetes, metabolic syndrome, tobacco use, activity and exercise level, coronary artery disease and related syndromes (e.g., angina, MI, stent, coronary artery bypass graft surgery, etc.); structural heart disease (e.g., cardiac valve disease, cardiomyopathy etc.), arrhythmias, peripheral vascular disease, cerebrovascular disease, and prior autonomic dysfunction. Presence of previous underlying pulmonary disorders should also be documented to help with differentiation of symptoms between cardiac and pulmonary etiologies.

If there has been a prior cardiovascular workup, a review of previously performed tests should be considered in the overall evaluation. Tests that may be available and helpful include blood tests (complete blood count [CBC], electrolytes, cardiac biomarkers [troponin, B-type natriuretic peptide], lipid panel etc.); electrocardiogram (EKG); chest imaging; echocardiogram (echo); heart rhythm monitoring; cardiac catheterization; stress testing. Cardiovascular treatment interventions to date should also be reviewed. If a patient is pregnant or of childbearing age, it is important to gather information

regarding any new or ongoing medical concerns (eg, menstrual cycles, likelihood of pregnancy, etc.).

Symptom characterization

A complete description of each PASC-related symptom is required, clarifying chronicity, course—improving, stable, regressing or fluctuating, and exacerbating or remitting activities. Screening is recommended for symptoms that are commonly reported by individuals with PASC and require differentiation from noncardiac causes:

1. **Chest pain**: In individuals with PASC, ongoing chest pain is common ranging from a prevalence in 10%–20% of patients 30–60 days after acute COVID-19 infection.[40] Chest pain in PASC has a broad differential including cardiac, pulmonary, musculoskeletal, gastrointestinal, and pain due to inflammation. The absence of chest pain does not exclude cardiac disease. Ischemic cardiac pain is mediated via the autonomic nervous system and can be absent in patients with autonomic neuropathy as is often seen in individuals with diabetes. Isolated dyspnea on exertion may also be a presenting feature of ischemia, especially in women. Chest pain worse lying down and improved sitting up and leaning forward can indicate pericarditis.
2. **Palpitations**: Up to 10% of individuals with PASC have reported palpitations—a heightened sense or awareness of the heartbeat.[41] In PASC, palpitations may be persistent or transient, at rest or only with activity.
3. **Dyspnea**: In individuals with PASC, dyspnea—the sense of "air hunger" or difficulty taking in a deep or satisfying breath—is reported in up to 30% of patients.[41] Dyspnea may be present at rest, on exertion, on lying flat (orthopnea), or wake an individual during the night (paroxysmal nocturnal dyspnea). Differentiating the cause of PASC-related dyspnea between heart disease, COVID-19 lung disease (including viral pneumonia, pulmonary fibrosis, pulmonary embolus), preexisting lung disease (chronic obstructive pulmonary disease), pain syndromes, anxiety disorder, deconditioning, or other etiologies is recommended. Characterizing breathing using standard measures of breathing discomfort can help direct the assessment and treatment plan as outlined in a prior PASC Collaborative Guidance statement on the assessment and management of breathing disorders.[42]
4. **Lower extremity edema**: New onset leg swelling has been reported in PASC. Leg swelling can be related to dependent edema in individuals who may be less active due to PASC symptoms. New onset of deep vein thrombosis in PASC is reported and can present with new onset or worsening of swelling. Leg swelling in individuals with PASC-related cardiovascular disorders may be indicative of declining cardiovascular function. Differentiating between congestive heart failure, cor pulmonale, deep vein thrombosis, venous insufficiency, lymphedema, dependent edema, liver disease, hypoalbuminemia, cellulitis, or other etiologies is indicated as management is cause dependent.
5. **Cough**: A new cough in PASC may be intermittent or persistent, dry or wet, productive of sputum or not and has been reported by 13% of individuals.[41] Differentiating between cardiac, obstructive or restrictive lung disorders, gastroesophageal reflux, postnasal drip, seasonal allergies, medication side effects, or other etiologies is important as the treatments vary.
6. **Fatigue**: Individuals with cardiovascular disease may report fatigue—a feeling of weariness, tiredness, or lack of energy. Fatigue in PASC has been addressed at length in a prior PASC Collaborative consensus guidance statement.[43] Differentiating cardiovascular fatigue from other causes in individuals with PASC, including fatigue in postexertional malaise is recommended as management is significantly different.
7. **Light-headedness**: Can be associated with syncope or presyncope, may be present at rest, sitting or lying, or only on standing and with activity and can be mild or severe. For patients with PASC, differentiating between cardiac causes (including arrhythmias, aortic stenosis, heart failure), vertigo, seizure disorders, vertebrobasilar insufficiency, anxiety/stress disorders, postural orthostatic tachycardia syndrome, orthostatic hypotension, or other etiologies is recommended.
8. **Dizziness:** Dizziness should be differentiated from light-headedness, as mentioned earlier. It is a nonspecific symptom that warrants further investigation to determine the etiology and referral to the appropriate specialist for management. Consider medications, cardiovascular, autonomic, metabolic, neurological, psychological, vestibular, cervicogenic, and visual pathologies. Dizziness that is accompanied by headache or other focal neurologic symptoms and signs should warrant a neurologic evaluation, as discussed in a forthcoming PASC Collaborative guidance statement on neurological sequalae in PASC.

It is important to note that cardiovascular disease related symptoms may coexist with other post-COVID-19 system disorders and related symptoms. It may not be possible to differentiate symptom etiology based on history alone.

Initial evaluation—physical examination

A thorough physical examination of the cardiovascular system should be performed in individuals with PASC with symptoms concerning for new onset of

cardiovascular disease or in those with a history of pre-existing cardiovascular disease where symptoms indicate an exacerbation. Elevated jugular venous pressure, ascites, and lower extremity edema may be associated with congestive heart failure in PASC. Signs such as pulsus alternans (associated with a pericardial effusion) may suggest ongoing post-COVID-19 inflammation and accumulation of fluid within the pericardial space and warrant referral to a cardiologist. Irregular arterial pulses may indicate atrial fibrillation—a common arrhythmia seen in PASC. New or worsening holosystolic or diastolic murmur, third (S3) or fourth (S4) heart sound, and loud (> II/VI) systolic murmurs may indicate new or worsening valvular heart disease due to PASC and should be referred to a cardiologist for formal evaluation. Any abnormalities detected should prompt further testing such as an EKG or echo and referral to a cardiologist.

To differentiate dizziness as a cardiovascular or neurologic symptom, vital signs should be done in a supine and standing position to evaluate for the presence of orthostatic heart rate and blood pressure abnormalities. A positional provocation exam, evaluating for the presence of benign paroxysmal positional vertigo or vascular dizziness includes a modified vertebral artery test, Dix-Hallpike maneuver for posterior canal pathology, and a roll test for horizontal canal pathologies. Further differentiation between primary balance disorders with *perceived* dizziness and conditions causing *actual* dizziness will be addressed in a forthcoming PASC Collaborative guidance statement on neurological sequelae in PASC.

If the cardiac examination is normal and there is a concern for a coexistent autonomic disorder, especially if there is an orthostatic variation in symptoms, consider performing a 10-minute stand test as discussed in the PASC Collaborative consensus guidance statement on autonomic dysfunction. (Blitshteyn S, Abramoff B, Azola A, et al. Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Autonomic Dysfunction in Patients with Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): submitted to PM&R, under review).

Initial evaluation—laboratory workup

In addition to the recommended baseline serum laboratory tests in PASC (CBC, basic metabolic/chemistry panel including magnesium [BMP]), thyroid stimulating hormone [TSH], and basic serum inflammatory markers (e.g., C-reactive protein) and erythrocyte sedimentation rate).[44] Specific cardiovascular labs can be considered based on presenting symptoms. Elevation of serum cardiac troponins is reported with COVID-19 related myocarditis, myocardial injury/ischemia, and infarction.[40] The level of troponin elevation is closely related to the severity of both myocardial injury and risk of cardiovascular mortality post infection.[45] Troponin elevation may also be associated with noncardiovascular complications including sepsis, acute kidney failure, and major bleeding.[46] In individuals with PASC with ongoing chest pain, a basic screening serum troponin, and EKG can be considered to confirm, or rule out, myocardial injury as a source of the chest pain and to determine the extent and severity of myocardial injury. Consider a high-sensitivity troponin assay if available as it can detect circulating troponin at lower levels and provide improved diagnostic clarity.[47] Because it remains unclear how long it takes for troponins to normalize in PASC-related myocarditis, an elevated "spot" troponin in individuals with PASC and chest pain may not indicate an acute cardiac event.

Differentiation between a cardiac or pulmonary origin of dyspnea in PASC can be facilitated with B-type natriuretic peptide (BNP) or N-terminal-pro-BNP (NT-pro-BNP)—markers of elevated cardiac pressure commonly used to screen for heart failure exacerbation. These markers can be significantly elevated in COVID-19 and are an independent marker of mortality risk.[48] Additionally, NT-pro-BNP and BNP are also markers of myocarditis in PASC. NT-pro-BNP or BNP can be included in focused cardiovascular testing in the workup of dyspnea in PASC.[49]

As COVID-19 infection is associated with thrombosis and thromboembolic events in patients with low to intermediate suspicion of venous thromboembolism, screening D-dimer is a reasonable tool to initiate the workup if intravascular thrombus is being considered.

If an autonomic disorder is being considered in conjunction with cardiovascular disease in causing PASC-associated arrhythmias (tachycardia, bradycardia), blood pressure lability, breathing disorders, and altered vascular tone leading to presyncope and syncope, additional laboratory tests for consideration include vitamin B12, thyroid screening including free T3, free T4, and TSH; morning cortisol; and serum ferritin.[50]

Initial evaluation—cardiac monitoring

EKG

A screening EKG is recommended to assess the heart rhythm, heart rate, timing and duration of the cardiac cycle, and any other underlying abnormalities (i.e., ST segment elevation or depression). If abnormalities are noted, comparison should be made to prior EKGs and referral to cardiology if new.

Clinicians familiar with ordering and responding to the results of the following tests may feel comfortable ordering themselves. If not familiar, then referral to cardiology is recommended if these tests are required.

Ambulatory cardiac rhythm monitoring
For patients reporting palpitations, short- or long-term cardiac monitoring can be considered to look at the heart rhythm over time and with activity variations. If not familiar with ordering and/or responding to abnormal results of ambulatory monitoring, referral to a cardiologist is recommended. For individuals with daily symptoms a 24- to 48-hour Holter monitor should suffice to identify arrhythmias. For those with infrequent symptoms, cardiac event monitors (looping or nonlooping depending on the duration of symptoms) may be required. Mobile cardiac telemetry patches are also available, can be worn for 2–4 weeks and record all arrhythmic events. Cardiac monitoring correlated with symptom event recording may help establish if the symptoms experienced are related to arrhythmias identified. For individuals with more infrequent symptoms, longer term monitoring over years is possible by implanting a loop recorder subcutaneously over the chest.

Echocardiogram (Echo)
For individuals with PASC with dyspnea or near syncope or syncopal episodes, a 2D transthoracic echocardiogram can be considered to identify structural abnormalities of the heart. If not familiar with ordering and/or responding to abnormal results on echo testing, a cardiology referral is recommended. Systolic and/or diastolic dysfunction of the left ventricle in PASC can contribute to dyspnea as well as predispose to arrhythmias leading to syncope. Note should be made of any cardiac valve abnormalities (ie, aortic stenosis, mitral stenosis, or regurgitation) that can contribute to dyspnea, chest pain, and syncope noted in PASC.

Cardiac stress test
For patients with PASC with chest pain or dyspnea on exertion suggestive of cardiovascular disease, cardiac stress testing can be considered. If not familiar with ordering and/or responding to abnormal results on cardiac stress testing, a cardiology referral is recommended. Exercise stress testing (EST) (treadmill or bike) with EKG or echo monitoring is the preferred choice as exercise provides more functional physiologic information on cardiac chronotropic competence, peak heart rate achieved and symptoms that may correlate with exertion. A pharmacologic stress test can be performed for those who cannot exercise to sufficient intensity for the stress test to be sensitive and specific—a heart rate of 80% of age and gender matched peak predicted. Contraindications to stress testing should be adhered to.[51]

For individuals with disabilities, the performance of cardiac assessments may need to be modified to achieve an effective evaluation. For example, upper extremity aerobic exercise testing may replace lower extremity exercise testing in people with paraplegia[52]; however, these tests require experience to interpret due to variability in cardiopulmonary responses.[53] Recommendations based on evaluation should be patient centered and address the goals of the individual. (Refer to Table 2: Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): Cardiovascular Complications).

Cardiologist co-management

Individuals with preexisting cardiac disease should follow up with their cardiologist for management of cardiovascular disorders in PASC. When an individual with PASC initially presents, the physician or evaluating clinician should assess for symptoms and signs suggestive of cardiovascular disorder and initiate the work up as per the guidance statement. With the identification of any new cardiovascular disorder, including unmanaged cardiovascular risk factors, new significant coronary artery disease, structural heart disease, new cardiac murmur, cardiomyopathy with diastolic or systolic dysfunction, or significant arrhythmia, referral to a cardiologist is indicated. It is implied throughout this guidance statement that such a referral is recommended when cardiovascular disorders in PASC are identified.

Cardiovascular disorders, postexertional symptom exacerbation, and activity/exercise considerations

Activity and exercise are recommended as part of standard of care for individuals with cardiovascular disorders. The "dosage" (duration, intensity, frequency) of activity and exercise is *prescribed* with consideration to medical stability and functional ability. In individuals with PASC and cardiovascular disorders, care must be taken to minimize or avoid postexertional symptom exacerbation, which has been well documented.[30,83] Postexertional symptom exacerbation should be considered whenever activity and exercise recommendations are made to individuals with cardiovascular disorders and PASC including in the following circumstances:

- patient evaluation with objective measures of activity performance including EST
- self-monitored progressive activity
- monitored cardiac rehabilitation
- progression toward athletic and sports participation

In the recommendations that follow in subsequent sections, consideration of postexertional symptom exacerbation should be guided by the following:

Mild to moderate postexertional fatigue or tiredness without other PASC symptom exacerbation, in proportion to the preceding "dose" of activity or exercise and

TABLE 2 Health equity considerations and examples in postacute sequelae of SARS-CoV-2 infection (PASC): Cardiovascular complications

Category	Comment	What is known	Clinical considerations
Biologic Sex *Example: Female adults*	Knowledge of areas of potential bias are important for clinicians to recognize and intentionally counteract in order to provide equitable healthcare.	Biologically female adults have some differences in cardiac risk factors as compared to male adults. For example, they go through menopause with ensuing physiologic changes (eg, hormonal, sarcopenia). Pregnancy has been reported to be a risk factor for more severe COVID-19 infection.[54]	Sex-related disparities have been reported and female adults may be underdiagnosed and undertreated for cardiac conditions, including referrals for cardiac rehabilitation.[55] Thus, it is important for clinicians to be aware of the potential for underdiagnosis or misdiagnosis and ensure that this group receives optimal care. Individuals with underlying and/or new PASC-related cardiac impairments should be considered for cardiac rehabilitation programs and referred in a timely manner. Pregnant individuals with baseline cardiac conditions and/or PASC-related cardiac conditions should be treated by clinicians who have expertise in this population as there are often contraindications with testing and treatment interventions that must be adhered to in order to protect the patient and fetus. Treating physicians should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and availability.
Disability *Example: People with certain conditions that cause disability and cardiac dysfunction*	Individuals with cardiovascular disease require special consideration in the workup and management of cardiac dysfunction in PASC. Further attention may be given for individuals with special needs and additional comorbidities.	People with disability due to spinal cord injury, stroke, and other common rehabilitation conditions are known to be at higher risk for cardiovascular disease. Many are also at higher risk for COVID-19 acute infection and/or more severe disease. The incidence of PASC-related cardiac sequelae has yet to be fully explored in patient populations with preexisting disability. However, clinicians should be aware of the overlapping issues of premorbid conditions associated with disability, risk of COVID-19 infection, severity of acute infection, and PASC sequelae. For example, patients with multiple sclerosis (MS) may be on disease modifying therapy (DMT), and both the MS and the DMT may put them at higher risk for COVID-19 acute infections as well as more severe course, though in a recent systematic review these were not consistent findings.[56] The review included more than 80 reports involving 2493 patients with MS and 37 patients with	The impact of PASC-related cardiac dysfunction should be considered in individuals with baseline comorbidities that involve disability. Cardiac assessments may need to be modified. For example, upper extremity aerobic exercise testing may replace lower extremity exercise testing in people with complete paralysis of the lower extremities[52]; however, these tests may be challenging to interpret because of variability in cardiopulmonary responses.[53] Treating physicians should determine whether the patient is referred for formal cardiac rehabilitation vs. other types of rehabilitation as the benefits, cost, and availability may vary, depending on a variety of factors. For safety purposes, patients may need to be cleared by a cardiologist prior to starting an exercise program. Safety precautions should be clearly documented and adhered to. Monitoring vital signs and pulse oximetry is important as is a patient's perceived exertion. Exercise and activity prescriptions, medications, injections, and other interventions aimed at supporting rehabilitation and enhanced function

(Continues)

TABLE 2 (Continued)

Category	Comment	What is known	Clinical considerations
		Neuromyelitis Optica Spectrum Disorder with COVID-19. Older age, higher expanded disability status scale (EDSS) scores, cardiac comorbidities, and obesity were independent risk factors for severe COVID-19.	should be tailored to the individual and prescribed by clinicians who are experienced in caring for medically complex patients.
Racial/ethnic minority groups *Example: People who identify as Black (including African-American), American-Indian/ Alaska Native, Pacific Islander, Asian-American, and Mixed Race, and/or Latino/ Hispanic (ethnicity)*	Individuals who identify with groups that have been historically, socially, or economically marginalized may be at higher risk for COVID-19 related morbidity and mortality.	Historically marginalized racial/ethnic minority groups have higher rates of COVID-19 infection and lower rates of access to health care services,[57] and these disparities are influenced by social determinants of health (SDOH).[58] The NACMI (North American COVID-19 and STEMI) registry demonstrated ST-segment elevation myocardial infarction (STEMI) in COVID positive patients disproportionately involving individuals from racial/ethnic minority groups (50%) with diabetes mellitus.[59,60]	Individuals from racial/ethnic minority groups have been reported to have lower referral rates to cardiac rehabilitation than people classified as White/Caucasian.[61] All individuals with cardiac impairment and cardiovascular disease such as heart failure or myocardial infarction (MI) should be considered for cardiac rehabilitation programs and referred in a timely manner. Treating physicians should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and availability. Every effort should be made to close gaps in health disparities and ensure optimal care for people who identify with racial/ethnic minority groups.
Insurance *Example: Individuals who are uninsured, underinsured, or cannot afford access to recommended healthcare services*	Insurance coverage, or lack thereof, should be considered when devising a treatment plan addressing cardiovascular issues in PASC. Encouraging patient engagement and addressing psychosocial factors may improve adherence with treatment recommendations.	States with the highest rates of the uninsured will have widening disparities in health outcomes among minority and low-income populations, worsening for those persons with PASC.[62] Lower participation in cardiac rehabilitation has been documented in older participants, women, patients with comorbidities, unemployed and uncoupled persons, less educated people, and those with lower income.[63] A similar pattern was observed for cardiac rehabilitation adherence. Also, those potential participants who live farther from cardiac rehabilitation facilities, do not have transportation, or do not drive, attended fewer rehabilitation sessions. Access to telehealth services may be helpful for health care access to individuals with challenges transportation, distance, and/or mobility.[64,65]	Clinicians should be aware of the cost of diagnostic and treatment interventions. Consider the value of diagnostic testing to rule in/out various conditions. Treatment interventions, such as physical therapy, may be limited by the cost of copayments and deductibles, even in patients who have medical insurance. Social services or community groups may assist persons with finding local support. Although access to telehealth services may facilitate care for some people, technology poses significant challenges for others. For example, individuals may have difficulty downloading, installing, and using new technology software or applications, a limited number of available digital devices, insufficient internet speed and bandwidth to manage audio and visual data, and poor quality of the camera and/or microphone on the device thus affecting the quality and diagnostic accuracy.[66] Insurance coverage for telemedicine services, including telephone visits and virtual visits online, has expanded during the pandemic—leading to greater use of these services. Telerehabilitation is often

(Continues)

TABLE 2 (Continued)

Category	Comment	What is known	Clinical considerations
			feasible[65] and patients have reported relatively high rates of satisfaction with physiatry[67] and therapy[68] visits.
Age *Example: Younger and older individuals*	Age should be considered in PASC-related cardiac conditions as this may affect clinical decision making.	Many clinical trials, including rehabilitation studies, have gaps in the inclusion of people across the age continuum, particularly children and older individuals.[69] Thus, clinicians should be aware that while PASC-related care needs will outpace the research for everyone, studies to guide the care of children and older individuals may be particularly slow to evolve. Nevertheless, studies are documenting issues such as multisystem inflammatory syndrome in children (MIS-C), also known as pediatric inflammatory multisystem syndrome, which is a potential complication in children recovering from COVID-19.[70] In a 1-year follow-up time period of a pediatric cohort, MIS-C associated cardiac manifestations included ventricular dysfunctions, pericarditis, coronaritis, and arrhythmias.[71] Fortunately, no subsequent cardiac anomalies were recorded on follow-up. Myocarditis is a potential complication of viral syndromes, including for young athletes returning to sport, especially as this is an important cause of sudden cardiac death during exercise.[72] A review in patients with type 2 diabetes mellitus and PASC highlighted issues related to older individuals.[73] The report explained that in diabetes, neuropathy and myopathy contribute to muscle atrophy and sarcopenia and acute COVID-19 infection, hospitalization, protein deficiency, and corticosteroid therapy often cause rapid onset sarcopenia in severe COVID-19 infections. Acute COVID-19 infection may also contribute to new or worsening cardiovascular issues.	To prevent serious cardiac sequelae, including sudden death in younger athletes, cardiac return to play pathways have been developed.[72,74] Low-risk patients should rest for at least 10 days after being diagnosed with COVID-19. If asymptomatic for 7 days, they can begin a gradual return to physical activity. Athletes with mild to moderate COVID-19 symptoms who fully recovered need a thorough assessment and history and physical examination. It is also recommended they have 12-lead electrocardiogram (EKG) and echocardiogram before return to play. If there are abnormalities, a cardiac magnetic resonance imaging (MRI) should be done to exclude myocarditis. Athletes with persistent COVID-19 symptoms who take longer than 14 days to recovery, are recommended to have a history and physical, 12-lead EKG, and cardiac MRI to check specifically for myocarditis. If the MRI is normal, then cardiopulmonary exercise testing and 23-h Holter EKG. These athletes cannot exercise maximally until initial investigations have been completed.[74] Athletes with preexisting disabilities should ideally be followed by sports medicine specialists (eg, physiatrists, physical therapists). If tests are abnormal in children and young athletes, a multidisciplinary team composed of specialists in cardiology, pulmonology, and sports medicine should collaborate to create a personalized exercise prescription for these patients. In older patients with type 2 diabetes mellitus, strict control of blood sugar and other comorbidities, supervised physical activity and exercise, and optimal nutrition may be helpful in reducing and managing PASC symptoms.[73] Because older individuals may have low skeletal muscle mass with baseline sarcopenia, following infection they may become weaker than premorbidly. Clinicians should be vigilant about recognizing new or worsening cardiovascular issues and cardiovascular stress with

(Continues)

TABLE 2 (Continued)

Category	Comment	What is known	Clinical considerations
			activity and/or exercise. For older individuals who have an upcoming surgery, prehabilitation may help to support optimal outcomes.[75] Virtual visits for telerehabilitation may enhance access to care for older individuals.[76]
Obesity *Example: People who are diagnosed as overweight/obese*	Obesity may not only increase the incidence and mortality associated with acute COVID-19 infection but also development of PASC-related symptoms.	Obesity is an important risk factor for the development of severe COVID-19 infection and mortality.[77] Moderate and severe obesity (body mass index [BMI] ≥ 35 kg/m^2) are associated with a greater risk of PASC.[77] In one study, PASC symptoms were characterized by fatigue, headache, dyspnea, and anosmia and these were more likely with increasing age, increased BMI, and female sex.[78] High BMI and previous pulmonary disease could be risk factors for development of PASC in exposed health care workers.[79]	Recognize that obesity as a comorbidity can increase a patient's risk for PASC and cardiac complications. There may also be associations with sympathetic overactivity and hypertension. Addressing weight loss strategies can be done within the patients' system of care and in consideration with their own SDOH. Obstructive sleep apnea is a common condition associated with obesity and should be addressed in order to optimize oxygenation and cardiac function as well as lessen fatigue. Exercise and physical activity should be appropriately prescribed and consider obesity as a comorbidity.
Justice Involved (Prisons/Detention Centers) *Example: People who are incarcerated or detained in prisons, jails, youth detention centers, immigration detention centers, internment camps, and other facilities*	People who are involved in some manner with various aspects of the criminal justice system, particularly those who are incarcerated in correctional facilities and detention centers, have a unique vulnerability to healthcare inequity that is often overlooked.	The proportion of COVID-19 cases is 5.5 times higher among people who are incarcerated.[80] Literature describes the impact of COVID-19 on confined communities (including people who are immigrating, seeking asylum or incarcerated) and offers practical recommendations on physical activity recommendations to maintain their level of independence, physical health, mental health and wellbeing.[78] Multiple factors contribute to a higher risk of cardiac disease in incarcerated women because of more cardiovascular health challenges.[81]	Cardiovascular disease is a leading cause of death among individuals incarcerated in correctional facilities.[82] After accounting for differences in racial identity and socioeconomic status, persons recently released from correctional facilities have a higher risk of being hospitalized and dying of cardiovascular disease compared with the general population.[82] Appropriate testing and treatment for cardiac sequela of COVID-19 should be accessible for individuals under correctional supervision.

Note: This table is included to provide additional information for clinicians who are treating patients for PASC-related cardiac complications. This is not intended to be a comprehensive list, but rather to provide clinical examples as they relate to health equity, health disparities, and social determinants of health. The literature demonstrates that all marginalized groups face socioeconomic barriers and access to care barriers, though these may or may not be barriers for a specific individual patient. People with intersectional identities (eg, those who identify with more than one underrepresented or marginalized group) often face enhanced levels of bias and discrimination.

lasting 12–48 hours can be expected in any individual who participates in unaccustomed activity and exercise and is indicative of deconditioning. Counseling should be provided to individuals with cardiovascular disorders and PASC as they initiate and progress the dose of activity and exercise performed to monitor for postexertional fatigue. Reassurance can be provided that postexertional fatigue is a "normal" response to unaccustomed activity and exercise, is expected, and will resolve.

More persistent, mild, moderate, or severe PEM with other PASC-symptom exacerbation (sense of fever, myalgia, joint stiffness, brain fog etc.), often out of proportion to the preceding "dose" of activity or exercise, is consistent with ME/CFS and may be seen in some individuals with PASC. PEM is often described as a "crash" and can last days, weeks, or months. Reducing the dosage of activity or exercise is required below that which precipitated the symptom exacerbation. The dose of activity and exercise

that can be performed regularly without subsequent PEM should be maintained until PEM and associated symptoms have resolved. Post-PEM recovery, recommendations to incrementally increase activity and exercise should be addressed in collaboration with the individual with PASC-associated PEM and with close monitoring for PEM symptom exacerbation.

Finally, individuals who do not tolerate upright activity because it exacerbates symptoms may benefit from recumbent, semirecumbent, and mat-level exercises of lower intensity and at shorter durations to reacclimate the cardiovascular physiology to appropriate systemic stress.

Measures of activity performance

Individuals with PASC who present with impaired activity tolerance or functional decline should be screened with objective measures of activity performance. These standardized functional tests should be individualized to the patient's functional abilities with modifications to accommodate comorbid orthopedic and neurological impairments, the presence of respiratory or autonomic features, and consideration of postexertional symptom exacerbation. During an initial office evaluation, consider in-office measures such as the 30-second sit-to-stand, 2-minute step test, and a 6-minute walk test.[84–89] Individuals with PASC who are unable to complete these standard assessments or perform below age-matched peers and those who report a decline in previous activity tolerance should be referred to a rehabilitation professional. Physiatrists and rehabilitation therapists can determine further testing to identify impairments contributing to the decline in activity and functional levels and plan appropriate rehabilitation therapy.

Standardized functional tests are done at the beginning and end of a therapeutic intervention and can be repeated during the rehabilitation course to quantify functional changes and determine appropriate training intensities to optimize therapeutic gains and return to prior functional levels. Monitoring vital signs at rest, during, and in the recovery period from functional testing, in conjunction with self-reported dyspnea on exertion or rate of perceived exertion scales, facilitates modification of the exercise prescription. Peak heart rates obtained from the functional tests can be used to assign safe and effective exercise targets. Clinicians should stipulate vital sign parameters when there is medical concern that warrants closer monitoring.

To provide a qualitative measure of functional activity tolerance, an EST can be performed on a treadmill—a cycle ergometer is acceptable if individuals are not able to complete a treadmill test. Metabolic equivalent (MET) levels achieved on a standardized EST protocol (Bruce, Modified Bruce, Naughton, etc.) correlate well with MET levels required for daily life activities—self-care/functional, avocational, and vocational. The EST is a requirement before starting a cardiac rehabilitation program, as well as facilitating risk stratification and mitigation of complications during cardiac rehabilitation. If available, a metabolic cardiopulmonary exercise test (CPET) facilitates an understanding of potential differential diagnoses of presenting symptoms—results can help differentiate between cardiac, pulmonary, and peripheral metabolic causes of symptoms and functional limitations. Repeating the EST or CPET (i.e., 6 months) or after cardiac rehabilitation allows objective evaluation of an individual's progress and can be correlated with symptom status.

TREATMENT RECOMMENDATIONS FOR CARDIOVASCULAR COMPLICATIONS OF PASC

Recommendations for the treatment of cardiovascular complications in patients with PASC are summarized in Table 3.

Discussion: Treatment of cardiovascular complications in individuals with PASC

Risk factor modification

Included in the primary goals of care for individuals with PASC is to improve patient function and restore quality of life. Management of cardiovascular disorders in PASC includes addressing modifiable cardiovascular risk factors. These include hypertension, dyslipidemia, diabetes, overweight/obesity, metabolic syndrome, tobacco use, and sedentary behavior.[90] It is important to note that some modifiable cardiovascular risk factors are also associated with increased morbidity and mortality in acute COVID-19, and emerging research is defining the role of their management in PASC.[91] Control of concomitant cardiovascular risk factors is likely to increase survival and improve symptomatic control in individuals with PASC.

Management of these risk factors is best implemented using a team-based approach, including the patient's primary care provider, and/or specialists such as a cardiologist or endocrinologist if available.[92] Using motivational interviewing to determine a patient's readiness for change in relation to modifying the risk factors may be useful. Tactful counseling based on motivational interviewing is recommended. Clinicians should be aware of and sensitive to social determinants of health as these may affect risk factors, particularly for people who identify with historically, socially, or economically marginalized groups. Many of the modifiable

TABLE 3 Recommendations for the treatment of cardiovascular complications in patients with PASC

	Cardiovascular complications treatment statement
1	Provide counseling and education for risk factor modification in individuals identified with risk factors for cardiovascular disease, including dyslipidemia, diabetes, hypertension, overweight/obesity, sedentary lifestyle, and depression. Education components can include: • Lifestyle modifications • Diet/nutrition • Activity/exercise • Medications • Risk factors • Disease process • Reassurance
2	Evaluate and manage individuals diagnosed with new or worse complex arrhythmias in conjunction with a cardiologist.
3	Evaluate and manage individuals diagnosed with new or worse structural heart disease in conjunction with a cardiologist.
4	Evaluate and manage individuals diagnosed with new or worsened coronary heart disease in conjunction with a cardiologist.
5	Evaluate and manage individuals diagnosed with new or worse ventricular dysfunction in conjunction with a cardiologist.
6	Individuals with a recent history of cardiac events and diagnosis that qualifies them for cardiac rehabilitation—myocardial infarction, stable angina, coronary intervention (percutaneous coronary intervention including angioplasty or cardiac stenting), systolic heart failure with ejection fraction ≤ 35%, heart surgery such as coronary artery bypass surgery, heart valve repair or replacement, and heart or heart-lung transplant—should be referred for cardiac rehabilitation.
7	Individuals with prior history of athletic performance should be evaluated, counseled, and guided back to sports performance through a staged return to play approach

Abbreviation: PASC, postacute sequelae of SARS-CoV-2 infection.

risk factors are closely interrelated and addressing one risk factor may positively affect others as well.

- Hypertension: Poorly controlled hypertension is associated with increased risk of severe COVID-19 and the development of PASC. The initial intervention to achieve optimal blood pressure (BP) goals includes increasing physical activity, weight management, restriction of sodium, and restriction of alcohol intake.[93] Medication management is initiated if lifestyle modification does not achieve BP goals within 3–6 months or if BP elevation is significant and is discussed in detail elsewhere.[94]
- Dyslipidemia: Although the direct effects of PASC on lipids is unclear, the relative inactivity and disability from the condition may cause changes. Initial intervention includes increasing physical activity, especially aerobic exercise and strength training, and dietary modifications as described later. Medications[94] may also be necessary for management of dyslipidemia, and working in conjunction with the patient's primary care provider and/or cardiologist is suggested.
- Diabetes: In addition to there being an increased incidence of severe COVID-19, cardiac mortality, and PASC in individuals with diabetes, the immobility and metabolic changes associated with PASC may cause impaired fasting glucose and diabetes.[95] Optimizing diabetic control reduces the incidence of MI, decreases cardiac interventions, improves quality of life, and improves survival rates in COVID-19 and PASC.[96] Diabetes management includes dietary modification and physical activity. Medication management may be required.[96] A team-based approach,working with the patient's primary care provider and/or endocrinologist is recommended.
- Overweight/obesity/metabolic syndrome: Overweight, obesity, and metabolic syndrome are associated with more severe COVID-19 and PASC and disproportionately affect people who identify with racial minority groups and may be linked to structural racism.[97–99] Obesity as a comorbidity can increase a patient's risk for PASC and cardiac complications. Moderate and severe obesity (body mass index ≥ 35 kg/m^2) are associated with a greater risk of PASC. Addressing weight loss strategies can be done within a patients' system of care and in consideration with their own social determinants of health. (Refer to Table 2: Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): Cardiovascular Complications) Initial treatment of overweight and obesity focuses on addressing physical inactivity and dietary modifications.[100]
- Tobacco Usage: Tobacco and tobacco product usage is associated with increased risk for severe COVID-19 and PASC and >30% of all cardiovascular-related deaths in the United States are due to tobacco use.[101] Smoking cessation counseling is central to initiating a reduction in tobacco-related cardiovascular and COVID-19/PASC related morbidity and mortality. A combination of behavioral support, nicotine replacement and bupropion provides the highest success rates for smoking cessation.[101] Individual or group behavioral counseling seems to be effective behavioral support.[102]
- Sedentary Behavior: Physical inactivity predicts cardiovascular morbidity and mortality as well as more severe COVID-19 and risk for PASC. Increasing energy expenditure through activity and exercise significantly predicts lower cardiovascular disease risk,[103] lowers low-density lipoprotein and triglycerides,[104] increases high-density lipoprotein,[105] reduces systolic and diastolic blood pressure,[106] improves diabetic control, facilitates weight loss, and increases likelihood of successful smoking cessation. Counseling to reduce sedentary behavior and increase overall activity levels in PASC is key in managing modifiable risk factors.

Those with symptoms of significant orthostatic intolerance may benefit from recumbent exercise such as recumbent cycling or rowing. Monitored activity and exercise in a cardiac rehabilitation setting should be prescribed if appropriate. When appropriate, exercise training may be a useful adjunct in increasing functional capacity and improving vascular endothelial dysfunction and reducing late thromboembolic complications in individuals with PASC.[106] A structured, symptom limited appropriately progressive and monitored exercise program may increase patient confidence that resumption of previous activities may be possible and safe.

- Diet/Nutrition: Potential barriers to adhering to a heart-healthy diet should be assessed, including food access and economic factors, which may be particularly relevant to individuals with PASC who are more likely to come from vulnerable populations. In general, a low sodium diet is recommended unless management of coexistent autonomic dysfunction supports the need for judicious sodium/salt supplementation. A diet emphasizing the intake of vegetables, fruits, legumes, nuts, whole grains, and vegetable sources of protein increases soluble and insoluble vegetable fiber intake and supports cardiovascular health, and in providing antioxidant and anti-inflammatory nutrients may well benefit other symptoms of PASC.
- Depression and stress: Psychological factors, such as depression and stress, are recognized as independent risk factors for coronary artery disease. Elevated rates of depression, stress, and anxiety are also reported in PASC. Screening for depression in patients in PASC with cardiovascular diseases is necessary because of an increased risk of mortality (relative risk 1.8).[107] The Patient Health Questionnaire (PHQ-9) and the 15-item Geriatric Depression Scale (for older adults) are commonly used and validated screening tools. If these screening tests are positive for depression, further evaluation is needed. A referral to the appropriate specialist is recommended to confirm the diagnosis and initiate and guide management. In addition, exercise training is an effective intervention to improve depression and stress in patients with heart disease.[108]

Management of cardiovascular disorders in PASC

Arrhythmias

Individuals with PASC experiencing palpitations may have atrial and/or ventricular ectopics (extra beats) identified with an ambulatory cardiac rhythm monitor. Noncomplex rhythms such as sinus bradycardia, sinus pauses, sinus tachycardia, and more concerning rhythms such as supraventricular tachycardia or ventricular tachycardia (sustained or nonsustained) may be identified. General management for arrhythmias includes removal of offending agents, such as avoidance of caffeine, alcohol, or other stimulants potentially contributing to the arrhythmia. More complex persistent or refractory arrhythmias requires antiarrhythmic drugs, ablation for refractory tachycardias, or permanent pacemaker for refractory symptomatic bradycardia or conduction system disorders. Arrhythmias including atrial fibrillation with hemodynamic consequences, frequent or multifocal ventricular complexes, nonsustained ventricular tachycardia or ventricular fibrillation, and heart block require more urgent or emergency referral and management.[109]

Coronary artery disease and coronary syndromes

Individuals with PASC identified with new nonocclusive CAD (<70% occlusion) require education and risk factor modification. Significant occlusive (>70%) CAD or symptomatic CAD (stable angina) requires more immediate or urgent (unstable angina/acute coronary syndrome) intervention. When individuals with PASC with CAD and or coronary syndromes are stable and medically cleared, referral to cardiac rehabilitation is indicated (discussed in a later section).

Ventricular dysfunction, structural heart disease, and heart failure in PASC

If heart failure is mild and the patient has minimal, no or stable symptoms, patients can be initially managed by primary care physicians in consultation with cardiology. Initial testing may include EKG, echo, and chest x-ray. Education for salt and water restriction can be initiated. If ventricular dysfunction and heart failure is more significant or symptoms (fatigue, dyspnea on exertion, cough, weight gain, leg swelling) are moderate or worsen, more immediate escalation is recommended. When individuals with PASC with systolic heart failure with an ejection fraction (EF) ≤ 35% are stable and medically cleared, referral to cardiac rehabilitation is indicated (see Medicare guidelines for heart failure referral to cardiac rehabilitation). Management of acute myocarditis is largely supportive and should be managed by cardiology. High intensity exercise or competitive sports participation should be restricted in patients with acute myocarditis. The finding of new heart valve abnormalities on echocardiography following COVID-19 is rare but the presence of angiotensin-converting enzyme 2 receptors on heart valves is a possible mechanism of acute heart valve disease following COVID-19 infection.[110,111]

Pulmonary embolism

COVID-19 is associated with a prothrombotic state and has been associated with pulmonary embolism.[33] Several case series have highlighted late acute pulmonary embolism after mild COVID-19 in otherwise healthy individuals.[112,113] Delayed recognition and diagnosis are associated with worse outcomes.[114] Echocardiography

results indicating RV strain supports the diagnosis of significant pulmonary embolism. Given this association, it is important for individuals with PASC with postacute symptom onset including acute central chest pain, unexplained tachycardia, dizziness, and palpitations, and/or abnormalities on echo be considered as possibly having pulmonary embolism and be evaluated expeditiously in an emergency department setting.

Cardiac rehabilitation

Individuals with PASC and cardiovascular disease that meet criteria qualify for and can be referred to a cardiac rehabilitation (CR) program. Cardiovascular diagnoses covered by insurance for CR and eligibility criteria for CR are discussed elsewhere.[115] Considering the impact of acute COVID-19 and PASC on the cardiovascular system, the following clinical scenarios qualify a patient for CR:

- evidence of an acute coronary event in the setting of COVID-19 with
  - elevated cardiac enzymes, or
  - new wall motion abnormalities noted on echo consistent with myocardial infarction, or
  - the need for coronary intervention with angioplasty or stent placement or coronary artery bypass grafting
- evidence of new myocardial dysfunction with EF ≤35%
- new heart valve disease requiring intervention - repair or replacement
- heart or heart-lung transplant following COVID-19 myocarditis

CR provides comprehensive long-term services involving medical evaluation, prescriptive exercise, cardiac risk-factor modification, education, counseling, and behavioral interventions for individuals with cardiovascular disorders.

For those with functional limitations due to PASC and cardiovascular disease that does not meet criteria to qualify for a formal CR program, or those with PASC and cardiovascular risk factors, education should be provided for a self-monitored symptom-guided progressive activity and exercise program. For individuals with more significant limitations of activities of daily living and overall function, a comprehensive outpatient rehabilitation program including occupational therapy and physical therapy should be considered. Notably, individuals who identify with racial or ethnic minority groups such as Hispanic/Latino and Black/African American may have less access to and/or experience other disparities regarding rehabilitation care, including CR. In addition, other aspects of health care disparity among Black and Hispanic populations with disability regarding rehabilitative services include fewer referrals, lower utilization rates, perceived bias, and more self-reliance, even after adjusting for hospital characteristics, age, disease severity, and relevant socioeconomic variables. Some studies found that Black individuals were less likely to receive care that was concordant with clinical guidelines per the reported literature.[116,117] Guidance in self-monitoring of heart rate response to exercise and the use of a subjective RPE scale to monitor exercise response and guide self-progression of intensity should be provided. A self-guided home exercise program should be multimodal including aerobic, resistance, and flexibility exercises with goals as detailed in the 2008/2018 Physical Activity Guidelines and include optimally 300 minutes a week of moderate intense aerobic exercise combined with resistance exercises two or more times a week.[118,119] Patients who have preexisting disability, poor health literacy, no previous exercise history, or who require vital sign monitoring with exercise-based interventions should be referred to a physiatrist for appropriate exercise prescription and modifications that can be implemented under the care of a rehabilitation therapist.

The structure and function of CR programs are well positioned to support individuals with PASC with qualifying cardiac diagnoses. CR is an effective means of mitigating disease and disability by establishing a plan to help introduce lifestyle changes, regain strength, and improve physical and emotional health and quality of life.

Educating individuals with PASC with cardiovascular complications who qualify for outpatient CR regarding the program is recommended as this improves participation and completion of the program. Following an evaluation by a CR trained physician (ie, a CR physiatrist or cardiologist) and a pre-CR program exercise test to guide the CR prescription, patients will attend CR 2–3 times a week for a total of 36 physician-supervised exercise sessions with a goal of 31–60 minutes of monitored aerobic exercise. In addition, individuals in a CR program receive education on cardiac health, risk factor modification, and nutrition. Supportive therapies are also available. On completion of the CR program the exercise stress test may be repeated to quantify physiologic progress and facilitate prescription of an ongoing self-monitored exercise program.

Individuals from racial/ethnic minority groups have been reported to have lower referral rates to CR than people classified as White/Caucasian.[61] As well, individuals from racial/ethnic minority groups are more likely to have COVID-19, severe COVID-19, cardiovascular disease risk factors and cardiovascular disease. Gender-related disparities have also been reported and female adults may be underdiagnosed and undertreated for cardiac conditions, including referrals for CR.[55] It is incumbent for clinicians to take into account the potential for underdiagnosis or misdiagnosis and actively address barriers such as cost and availability to support health equity. Pregnant

women with baseline cardiac conditions and/or PASC-related cardiac conditions should be treated by clinicians who have expertise in this population as there are often contraindications with testing and treatment interventions that must be adhered to in order to protect the mother and fetus. (Refer to Table 2: Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): Cardiovascular Complications).

At home CR programs are an option that may facilitate participation in a CR program, depending on insurance coverage.[120]

Contraindications to cardiac rehabilitation participation

Contraindications to CR participation are similar for PASC patients, are well documented and will be identified by the CR program medical director.[121]

Patients who do or do not qualify for CR who have concomitant COVID-19-related myocarditis should be delayed from starting CR or a self-monitored exercise program for 3–6 months. If no arrhythmias or ventricular dysfunction (normal EF) have been documented, light and slowly progressive exercise can be started closer to 3 months. If the patient has abnormal ventricular function (abnormal/low EF), patients are not cleared to exercise and should be reevaluated at 6 months to assess improvement in EF. Once cleared to exercise and participate in CR the exercise "dose" can be slowly increased to desired levels, the exercise progression guided in part by symptoms including dyspnea and fatigue.

Indications to terminate a CR exercise session include any significantly distressing symptoms, chest pain indicative of angina/ischemia, poorly controlled and/or complex arrhythmias, severe dyspnea, lightheadedness, presyncope or syncope, or excessive fatigue.

For individuals with coexistent pulmonary impairment, monitoring of oxygen saturation, and appropriate use of supplemental oxygen may be required if saturations drop below 90% with exercise. It is important for individuals with PASC who may have both cardiac and pulmonary limitations to be considered for inclusion in cardiopulmonary rehabilitation programs. Qualifying criteria for and details of pulmonary rehabilitation are detailed in the Collaborative's Consensus Guidance Statement on Breathing and Respiratory Sequelae.[42]

Some individuals with PASC who qualify for CR will also require other rehabilitative services (physical therapy, occupational therapy, speech therapy) for coexistent physical and functional limitations. Treatment interventions, such as CR and physical therapy, may be limited by the cost of copayments and deductibles, even in patients who have medical insurance. Availability of providers may also limit access to healthcare in certain geographical areas. Social services or community groups may assist persons with finding local support. (Refer to Table 2: Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): Cardiovascular Complications).

Cardiovascular considerations of the athlete and return to play

Management of the athlete with a COVID-19 related cardiovascular disorder should be guided by both a symptom-oriented and a disease-oriented approach. The psychological burden of withholding an athlete from participation in team activity, return to play, and the cost of overmedicalization must be considered.[121] Most elite and professional athletes are subject to preparticipation cardiovascular evaluation protocols established by their governing federations. Abnormal cardiac and respiratory results in athletes with PASC and cardiovascular disorders should be followed by a restriction of training as the athlete undergoes further cardiorespiratory evaluation. Management of the most common PASC-related cardiovascular conditions, including cardiomyopathies, ischemic heart disease, and arrhythmias should follow current guidelines. Athletes with normal results should follow a graduated return to training based on symptom response with reassessment every 24 hours.[121] The 2022 Expert Consensus from the American Academy of Cardiology (ACC)[47] recommends athletes may resume exercise training when the following criteria have been met:

1. Recent SARS-CoV-2 infection, who are asymptomatic and have abstained from exercise for 3 days during self-isolation
2. Recent SARS-CoV-2 infection who experienced mild or moderate noncardiopulmonary symptoms, which have resolved
3. Remote infection >3 months ago without ongoing cardiopulmonary symptoms and require no additional testing

Athletes who report ongoing cardiopulmonary symptoms, those who develop new cardiopulmonary symptoms after resuming exercise training, and/or those requiring hospitalization with heightened suspicion for cardiac involvement should undergo the recommended triad testing of EKG, cardiac troponin, and echocardiogram and be managed accordingly. Additional testing may include maximal-effort exercise testing and consideration of ambulatory rhythm monitoring may be beneficial in athletes with persistent cardiopulmonary symptoms and normal CMR findings or CMR findings of previous myocardial/pericardial involvement once myocarditis has been excluded.[47]:

Although initial reports indicated a high prevalence of COVID-19-related CMR imaging abnormalities (78%) in ambulatory adults,[122] recent data are more

encouraging. Data from larger registries of professional (N = 789) and collegiate athletes (N = 3018) tracked as they recovered from COVID-19 infections with conservative guidelines reveal a low prevalence of myocarditis on CMR (0.6%–0.7%) with no adverse cardiac events following return to sports participation.[123,124]

CMR studies in younger, healthier, and previously fit populations have been reassuring, although a wide range of findings may still exist. Rates of active myocarditis in young athletes have been reported from zero[125] to 15%,[126] and isolated areas of myocardial fibrosis, suggestive of previous injury, from 19%[125] to 30%.[126]

Athletes diagnosed with myocarditis should undergo a resting echocardiogram, 24-hour Holter monitoring and an exercise 12-lead EKG no less than 3–6 months following illness prior to return to sport. Training may be resumed if the following criteria are met: ventricular systolic function has normalized; serum markers of myocardial injury, heart failure, and inflammation have normalized; clinically relevant arrhythmias on Holter monitoring and graded exercise 12-lead EKG are absent.[127] A period of relative rest should be dependent on clinical severity and duration of myocarditis or associated illness, and athletes should undergo periodic reassessments following return to sport for the first 2 years owing to the risk of silent clinical progression.[128]

A staged return to play is best achieved in collaboration with professionals skilled in sports exercise prescription including sports medicine physicians, exercise physiologists, sports physical therapists and athletic trainers. Sports participation should be accomplished with consideration of training duration and intensity, using percentage of predicted heart rate max or actual heart rate max from an EST and/or subjective perceived levels of exertion. Practical tools for clinicians to use when prescribing sports exercise and guidelines for exercise testing and prescription have been previously developed by the American College of Sports Medicine (ACSM)[117]:

- ACSM Physical Activity Vital Sign available at: https://exerciseismedicine.org/wp-content/uploads/2021/04/EIM-Physical-Activity-Vital-Sign.pdf
- ACSM Tips for Monitoring Aerobic Exercise Intensity available at: https://www.acsm.org/docs/default-source/files-for-resource-library/exercise-intensity-infographic.pdf?sfvrsn=f467c793_2

Return to sport activity prescriptions and guidelines are available for use in healthy individuals or those returning to activities once acute medical issues have resolved and the patient is clinically stable. Where indicated, clinicians requiring assistance in interpretation of vital signs for return to activity a referral to a clinical exercise physiologist or physical therapist for appropriate activity prescription should be considered. Specifying vital sign parameters for training intensities when referring patients to sports trainers can be considered according to the ACC 2022 Expert Consensus.[45] Note the existing literature on athletes return to exercise and play is generally not aimed at providing guidance for people with a preexisting disability (eg, athletes with spinal cord injury) or comorbidities. Athletes with disabilities, such as spinal cord injury, limb loss, and other neurologic conditions, have unique physical, functional, athletic, and medical needs requiring a more specialized approach to sports participation. Referral to sports medicine physiatrists should be considered for athletes with disabilities and PASC-related cardiovascular disorders to help optimize the successful return to optimum sports participation while minimizing risk of injury or unexpected/atypical hemodynamic responses.

Contraindications to athletic and sports participation

Individuals with PASC with active myocarditis should refrain from athletic and sports participation until cleared by cardiology to participate. Further details of the evaluation, management, and treatment of myocarditis in athletes is beyond the scope of this guidance statement and has been reviewed elsewhere.[130] Myocarditis is with cardiac dysfunction and arrhythmias and is one of the leading causes for sudden cardiac death in athletes. Physical exertion is a trigger for dangerous arrhythmias and may further propagate myocardial damage in athletes with myocarditis. Establishing a stepwise approach for proper diagnosis and risk stratification using CMR imaging in myocarditis is critical. After a diagnosis of myocarditis is made, it is imperative for any athlete or highly active individual to refrain from physical exercise until resolved or cleared by cardiology to resume.

FUTURE DIRECTIONS

The etiology of PASC is still to be elucidated and at this time there is no specific evidence-based treatment of PASC symptoms and conditions including cardiovascular disorders. Numerous research initiatives are underway to better understand the pathogenesis of PASC and the outcomes of these studies should help guide management of cardiovascular conditions in individuals with PASC. Improved control of cardiovascular risk factors including diabetes, hypertension, obesity, tobacco use, and physical inactivity in individuals otherwise at high risk for more severe acute COVID-19 is likely to improve outcomes in acute COVID-19 including acute cardiovascular conditions but data to support this hypothesis are not yet available. The majority of individuals with PASC related

cardiovascular complications were infected with the alpha and delta COVID-19 variants pre-COVID-19 vaccination or vaccine booster and it is yet to be seen if PASC and related cardiovascular complications will be as prevalent or significant in individuals infected with different variants and fully vaccinated. Health care disparities have also been noted to impact the severity of acute COVID-19 and prevalence of PASC in the same populations at risk for cardiovascular diseases. It is yet to be seen if efforts to improve health equity in vulnerable populations will have a positive impact on the cardiovascular complications in PASC (Table 3).

HEALTH EQUITY STATEMENT

The AAPM&R recognizes the need to support equitable access to rehabilitation care for individuals with PASC. The AAPM&R states that equitable access to care includes (1) timely and local patient access to multidisciplinary care; (2) addressing inequities in the U.S. health system that result in diminished access to sustained quality care because of structural racism or socioeconomic factors; and (3) strengthened safety-net care, including disability evaluation and benefits.[131]

Each of the AAPM&R's PASC guidance statements were produced by a diverse and multidisciplinary team of subject matter experts with patient input. Although an in-depth discussion of health equity issues is beyond the scope of the PASC guidance statements, each one highlights health equity concerns and refers readers to other publications and resources. The term "health equity" has many different definitions, and they generally focus on ensuring that every person is able to achieve the highest level of health and function. For example, the Centers for Disease Control and Prevention defines health equity as the opportunity for people to fulfill their full health potential and states that people should not be disadvantaged from achieving their potential because of social position or other socially determined circumstances.[132] The Centers for Medicare and Medicaid Services uses the definition established in Executive Order 13985, issued on January 25, 2021 that states equity is "the consistent and systematic fair, just, and impartial treatment of all individuals, including individuals who belong to underserved communities who have been denied such treatment, such as Black, Latino, and Indigenous and Native American persons, Asian Americans and Pacific Islanders and other persons of color; members of religious minorities; lesbian, gay, bisexual, transgender, and queer (LGBTQ+) persons; persons with disabilities; persons who live in rural areas; and persons otherwise adversely affected by persistent poverty or inequality."[133] There are many root causes for health disparities, some of which fall under the categories within social determinants of health (SDOH). Examples of SDOH include but are not limited to socioeconomic status, neighborhood, availability and access to healthy food, and access to a high-quality education.

In addition to advocating for equitable access to rehabilitation care for all persons with PASC, the AAPM&R supports four "Principles of Inclusion and Engagement" that include (1) valuing diverse group composition (a diverse group is more representative of AAPM&R's membership and volunteers may be selected as a member of a particular community to enhance diversity of thought and experiences); (2) mutual respect (cultivating a receptive space for differing opinions and viewpoints); (3) talent and skill-based selection for leadership opportunities (ensuring that broad criteria of diversity of experience, talent and knowledge are incorporated and removing barriers to involvement that support an equitable environment); and (4) comprehensive collaboration (building community among various member constituent and bringing together different perspectives).[134] Readers of the PASC guidance statements are encouraged to consider the recommendations through the lens of health equity in order to improve access to rehabilitation care for all individuals with PASC.

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CME Question

Which serum marker can facilitate differentiating between dyspnea of cardiac or pulmonary origin in patients with post-acute sequelae of SARS-CoV-2?
a. D-dimer
b. Hemoglobin
c. Angiotensin converting enzyme
d. B-type natriuretic peptide
Answer online at https://onlinelearning.aapmr.org/

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