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Invited Review

COVID-19, cardiac involvement and cardiac rehabilitation: Insights from a rehabilitation perspective - State of the Art

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ABSTRACT

Since the beginning of the pandemic, many novel coronavirus disease 2019 (COVID-19) patients have experienced multisystem involvement or become critically ill and treated in intensive care units, and even died. Among these systemic effects, cardiac involvement may have very important consequences for the patient's prognosis and later life. Patients with COVID-19 may develop cardiac complications such as heart failure, myocarditis, pericarditis, vasculitis, acute coronary syndrome, and cardiac arrhythmias or trigger an accompanying cardiac disease. The ratio of COVID-19 cardiac involvement ranges between 7 and 28% in hospitalized patients with worse outcomes, longer stay in the intensive care unit, and a higher risk of death. Furthermore, deconditioning due to immobility and muscle involvement can be seen in post-COVID-19 patients and significant physical, cognitive and psychosocial impairments may be observed in some cases. Considering that the definition of health is "a state of complete physical, mental and social well-being", individuals with heart involvement due to COVID-19 should be rehabilitated by evaluating all these aspects of the disease effect. In the light of the rehabilitation perspective and given the increasing number of patients with cardiac manifestations of COVID-19, in this review, we discuss the rehabilitation principles in this group of patients.

Keywords: Cardiac disease, cardiac rehabilitation, cardiovascular, COVID-19, SARS-CoV-2.

Manifestations of the cardiovascular system of novel coronavirus disease 2019 (COVID-19) have attracted attention through multi-facet cardiac symptoms, clinical features, and sudden cardiac events. According to the two-year experience, in nearly half of the patients, cardiovascular system has been affected even with or without clinical features of respiratory disease.[1] Fu et al.[2] found that up to 23% of hospitalized patients with COVID-19 suffered from a cardiac injury.

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PATHOPHYSIOLOGY OF CARDIAC INVOLVEMENT OF COVID-19

Throughout the literature regarding the pathophysiology of cardiac and vascular involvement, seven main reasons have been discussed. These can be explained as follows:

1. Direct viral effect on the tissues, which is mainly benign, but named as elimination phase and responsible for the elimination of the virus from the tissues. This possible mechanism directly involves viral infiltration onto the myocardial tissue.
2. Excessive inflammatory effect (cytokine release syndrome), which is mainly known as storm-like phase, leads to severe inflammation of the targeted cells (such as lung, heart, endothelial, lymphoid tissue, pancreas, kidney) by interleukin (IL)-2, IL-6, IL-8, IL-10, and tumor necrosis factor (TNF). These cytokines play an essential role in myocardial cell injury, and also the cardiometabolic demand associated with the systemic infection and ongoing hypoxia-induced excessive intracellular calcium and cardiac stress lead to respiratory failure and hypoxemia.
3. Crosstalk between coagulation and inflammation is evident. Endothelial dysfunction shifts the vascular equilibrium toward an inflammatory and pro-coagulant state which tends to thrombosis and vasculitis.
4. Unmanageable cascade of hyper-inflammation may transform into an autoimmune overreacted response.
5. Sepsis, which leads to the development of disseminated intravascular coagulation syndrome.
6. Electrolyte imbalance
7. Side effects of medical treatment during hospitalization.[2,3]

Cardiovascular involvement during the course of the disease can be divided into two periods. One is acute sequelae, seen at the very early stage of the infection (from the incubation to four weeks), and the other is post-acute sequelae, seen after the fourth week of the infection (Table 1). According to the organ (heart) and its components (pericardium, myocardium, coronary arteries) injured, the clinical picture emerges as arrhythmia, myocardial infarction (MI), myocarditis, pericarditis, acute coronary syndrome, heart failure (HF) (acute onset and exacerbation of chronic HF) and post-acute sequelae coronary vascular disease (PASC-CVD), post-acute sequelae-cardiovascular symptoms (PASC-CVS), blood pressure dysfunction, postural orthostatic tachycardia syndrome (POTS), and myalgic encephalomyelitis (Table 1).[1,4]

INJURIES AND CLINICAL PRESENTATIONS

Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) virus has specific injury sites for the heart:

Pericardial injury: Pericarditis with pericardial effusion, cardiac tamponade, and myopericarditis in COVID-19 infection is a well-known entity and has a prevalence of 1.2% in adults.[5] Although pericarditis is not as common as other cardiovascular involvements, it can be added to the clinical picture during or after infection. The most common findings on electrocardiogram (ECG) are diffuse ST elevation (mostly concave type) and PR depression with fewer focal T wave inversion.[6]

Myocardial injury: The most common cardiac complication of COVID-19 is acute cardiac injury defined as measured elevated cardiac troponin above the 99th percentile of the upper reference limit or the presence of new ECG or echocardiographic abnormalities. Myocardial injury in COVID-19 may be associated with both ischemic disorders, such as acute MI (AMI) and non-ischemic disorders such

TABLE 1
Cardiovascular involvement after COVID-19 infection

Acute sequelae: Arrhythmia, myocardial infarction, myocarditis, pericarditis, acute coronary syndrome, heart failure (acute onset and exacerbation of chronic heart failure)
Post-acute sequelae: Post-acute sequelae coronary vascular disease (PASC-CVD), post-acute sequelae-cardiovascular symptoms (PASC-CVS), blood pressure dysfunction, postural orthostatic tachycardia syndrome (POTS), myalgic encephalomyelitis (chronic fatigue syndrome)

as myocarditis, Takotsubo syndrome, and acute HF due to systolic or diastolic dysfunction. Incidence of cardiac injury in COVID-19 patients has been shown to range from 6 to 25%.[7] The development of cardiac injury is observed more frequently in cases with hypertension and coronary artery disease.

Endocardial injury: In addition to the function of the endocardium as a layer of chambers, it contains the conduction system and is responsible for their proper functioning. Endocardial injury caused by the infection is a controversial issue. There are few reports in the literature regarding cardiac arrhythmia that may be caused by endocardial injury demonstrated by endocardial biopsy.[8]

Common clinical presentations of myocardial injury

Myocardial infarction Due to extensive inflammation and hypercoagulability, patients with COVID-19 are at risk of developing AMI. Acute MI, including ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI), defines myocardial damage resulting from acute ischemia of the myocardium. The diagnosis of AMI is based on the presence of one of the criteria for myocardial ischemia symptoms, new ischemic ECG changes, development of pathological Q wave, detection of new loss of viable myocardium or new segmental wall motion abnormality, and the presence of thrombus demonstrated by angiography or autopsy with elevated cardiac troponin levels.[9] Although the available data are limited, it is thought that the massive systemic inflammatory response in COVID-19 may trigger plaque rupture and thrombosis leading to type 1 AMI. Fever, hypoxia, tachycardia, and the hyperdynamic state due to excessive sympathetic stimulation may also cause demand-supply mismatch leading to type 2 AMI.[10]

It should be kept in mind that symptoms of AMI in patients with COVID-19 may mimic myocarditis or pericarditis and these patients may not present with typical angina symptoms. Moreover, acute myocarditis in COVID-19 patients may develop transient ST elevation that resolves later without any intervention. Detection of widespread ST elevations without reciprocal ST depressions on ECG usually suggests myocarditis. However, clinical suspicion of myocarditis should be maintained in COVID-19 patients presenting with focal ST-segment elevation. The American College of Cardiology (ACC) recommends that the diagnosis and treatment of STEMI and NSTEMI in patients with known or suspected COVID-19 should be approached in the same way as those without.

Myocarditis is an inflammatory disease characterized by inflammation of the myocardium in the absence of a predominant acute or chronic ischemia characteristic of coronary artery disease.[11] The damage is usually multifocal within the myocardium, and occurrence of arrhythmias and progression to severe left ventricular dysfunction and myocarditis can lead to fulminant HF, cardiogenic shock, and death. The prevalence of myocarditis in patients with COVID-19 is unclear due to the difficulties in precise diagnosis. Symptoms such as fatigue, dyspnea, and chest pain are commonly seen. Tachycardia during rest is a significant finding for myocarditis. Increased jugular venous pressure, peripheral edema, and right upper quadrant pain are the main hallmarks of right ventricular failure. Cardiac troponin levels, ECG, and transthoracic echocardiography (TTE) are useful diagnostic tools. Elevation of cardiac troponin with N-terminal pro B-type natriuretic peptide (NT-ProBNP) is frequently observed in these patients in contrast to ischemic injury in which mainly troponin increase is seen. In these cases, ischemia can be ruled out in this regard. While troponin seems to be a marker of worse prognosis and mortality, concomitant increased levels of leukocytes, D-dimer, C-reactive protein (CRP), ferritin, and IL-6 may also play an important role in inflammatory hyperactivity and myocardial injury in patients with COVID-19.[12] Sinus tachycardia and non-specific ST/T-wave changes are the most frequently seen ECG changes in myocarditis. New-onset bundle branch block, QT prolongation, ventricular extrasystole, and atrioventricular block are the other types of arrythmia seen in these patients. Also, TTE is helpful in the diagnosis. Cardiac computed tomography may serve to exclude coronary artery disease. If available, cardiac magnetic resonance imaging (MRI) helps to make the correct diagnosis. If the diagnosis still remains unclear, endomyocardial biopsy may help to identify myocardial involvement.

Stress-induced cardiomyopathy (Takotsubo cardiomyopathy) is also seen in COVID-19 patients. It is characterized by transient weakening of myocytes, particularly in the apex of the heart, which is typically represented by apical ballooning. It is thought that not only direct effect of the virus on cardiomyocytes, but also the profound emotional stress caused by long-term isolation period leading to an excessive release of catecholamines may be an additional factor in the occurrence of Takotsubo cardiomyopathy.[12] Marked elevations in cardiac troponins (i.e., >5 times higher

than the normal range) may indicate the presence of severe myocarditis or Takotsubo cardiomyopathy.

New-onset HF is observed in quarter of all hospitalized patients; and in one-third of patients who were in the intensive care unit (ICU).[13] In a meta-analysis of 40 studies, the overall ratio was given as 19%.[14] Systemic inflammation may trigger myocardial injury, myositis necrosis, and acute HF. Ischemic-induced inflammation and myocyte necrosis can also lead to immune cell infiltration, activation of fibroblasts, scar tissue formation, and replacement of dead heart tissue by fibrotic scarring. Increasing stiffness of the heart walls over time can lead to left ventricle diastolic dysfunction and HF. Another cause for the existence of acute HF is respiratory failure and hypoxia, which can increase myocardial energy demand in the patient.

Exacerbation of preexisting chronic HF It is known that viral infections such as influenza can exacerbate preexisting HF. Patients infected with COVID-19 have a higher risk of acute decompensation and these patients are more likely to die during hospitalization compared to those without a diagnosis of HF. Cytokine storm, coagulation abnormalities, and thrombotic events are thought to be important factors that may exacerbate preexistent HF.[12]

Atrial and ventricular arrhythmias have been observed in infected patients. New-onset arrhythmias can be seen in 5.3 to 13.3% of patients, and this ratio increases up to 44% in severe cases. Arrhythmias occurring during hospitalization are present in a range between 7.2 and 26.5% of patients.[15] The common type of arrhythmias reported among patients with SARS-CoV-2 includes sinus tachycardia, atrial fibrillation, atrial flutter, ventricular tachycardia, ventricular fibrillation, and bradycardia with high-degree atrioventricular block and pulseless electrical activity which is named cardiac arrest.

Blood pressure abnormalities can be seen after COVID-19 infection. Renin-angiotensin aldosterone-angiotensin-converting enzyme-2 is a key counter-regulatory enzyme that acts on blood pressure normalization. Hypotension, in the form of the postural orthostatic hypotension accompanied by tachycardia, is more frequent than hypertension attacks.[16]

Post-acute cardiovascular sequelae of SARS-CoV-2 infection (PASC) is a heterogeneous disorder without a universally accepted definition for its widely varying presentations which may begin at four to 12 weeks following the infection. Its incidence is reported as 10 to 15% in all infected population including mild disease. Nearly all patients had cardiovascular symptoms (85%) such as tachycardia, dyspnea, chest pain, palpitations, fatigue, sleep disturbances, and cognitive disturbances. It has four main types:

1. **PASC-CVD:** It defines at least one cardiac disease related to COVID-19 (such as myocarditis, pericarditis, myocardial ischemia, HF, thromboembolism, arrhythmia, pulmonary hypertension) and covers 15% of patients with cardiac manifestations.
2. **PASC-CVS:** It defines the symptoms that are related to cardiovascular diseases. The incidence of PACS-CVS patients is 85% of all PACS patients. Exercise intolerance and tachycardia are the uppermost symptoms. The time for treatment of these symptoms depends on the duration and severity.
3. **POTS:** It is an autonomic dysregulation which is one of the post-acute sequela syndromes of infection. Patients with POTS usually have a heart rate >30 bpm above the supine heart rate after 5 to 10 min of quiet standing, palpitations, lightheadedness, weakness, fatigue, blurry vision, and exercise intolerance. Other types of arrhythmias and rhythm-related conditions should be kept in mind in the differential diagnosis.[1]
4. **Myalgic encephalomyelitis (chronic fatigue syndrome):** It is difficult to generate the definition. Patients with extensive lung injury, requirement for mechanical ventilation, and/or serious cardiovascular complications may experience protracted sequelae related to the initial insult.

Biomarkers

Troponin I/T: Elevation of troponins was reported to vary between 7 and 36% in hospitalized patients with COVID-19.[17] Elevation of troponins can be classified as: ***(i)*** **Mild troponin elevation** (2 to 3 times higher than the normal range): This was the most common pattern and such mild elevations can be explained by the combination of possible pre-existing cardiac disease or cardiac injury. ***(ii)*** **Moderate troponin elevation** (3 to 5 times higher than the normal range): These groups of patients are at risk of developing myocarditis or stress cardiomyopathy. ***(iii)*** **Marked troponin elevation** (>5 times higher than the normal range): This may indicate the presence of severe

respiratory failure, systemic hypoxemia, myocarditis, stress cardiomyopathy or acute coronary syndromes.

B-type natriuretic peptide (BNP) and N-terminal pro B-type natriuretic peptide: Both biomarkers have been shown to be increased during hemodynamic myocardial stress and HF. In the follow-up period, measurement of both biomarkers may give useful knowledge about the status and course of HF.[18]

D-dimer: It is a fibrin degradation product and its main utility is in the diagnosis and management of arterial thromboembolic events. D-dimer may also be elevated in infections and inflammatory conditions. D-dimer may be associated with the progression of infection and poor outcome.[18]

Lactate dehydrogenase (LDH): High LDH levels reflect organ injury resulting from decreased oxygenation and can be a useful predictor of worsening prognosis in patients with COVID-19.[19]

GOALS AND OBJECTIVES OF CARDIAC REHABILITATION (CR) IN CARDIAC INVOLVEMENTS OF COVID-19

The role of comprehensive CR in improving functional capacity, well-being, quality of life (QoL) and reducing cardiovascular mortality and morbidity is well established. Cardiac rehabilitation is Class IA recommendation by the American Heart Association (AHA) as the first step in the secondary prevention of cardiovascular diseases.[20]

The main objectives of CR in cardiovascular involvements of COVID-19 are to reverse the physiological and psychological effects of cardiovascular diseases including endothelial dysfunction, to optimize cardiovascular risk management, to provide clinical stability, to reduce adverse cardiovascular events and hospitalizations, to improve functional capacity, psychosocial, occupational status and to decrease the health-related economic burden.

Components of cardiac rehabilitation

Comprehensive CR programs include all key components such as patient assessment and education, management of cardiovascular risk factors, cessation of smoking, counseling for daily living activities, sleep hygiene and physical activity (PA), exercise training, nutritional counseling and advice, psychosocial counseling and management, occupational therapy, and vocational support.[21] Exercise training is the cornerstone of CR. Respiratory muscle training should be included in the exercise program of patients with ongoing respiratory symptoms such as cough as a part of long COVID-19 syndrome.

Exercise has been proven to have immediate positive results for the heart and coronary vasculature, including myocardial oxygen demand, endothelial function, coagulation, inflammation and formation of collateral coronary arteries.

Indications and contraindications of CR following cardiac involvement due to COVID-19

Patients with cardiovascular involvements due to COVID-19, preexisting heart diseases with progressive symptoms following COVID-19 and cardiovascular symptoms (such as palpitations, dyspnea, fatigue) of long COVID-19 are candidates for CR. Presence of symptoms, limitations in function and restrictions in social roles related to cardiac diseases are indications for CR in these patients.

Indications and contraindications of exercise training specific to COVID-19 cardiac involvements apply to the well-known CR guidelines and recommendations. Some special conditions related to COVID-19 are mentioned in Table 2 and Table 3. Clinical, hemodynamic and rhythmic stability is required for all diagnosis.

EVALUATION OF COVID-19 PATIENTS WITH CARDIAC INVOLVEMENT

First, it should be emphasized that a holistic approach to all body systems is an important step in formulating an individualized CR plan. Before the inclusion of patients to CR program, the extent of cardiac damage, amount of myocardial ischemia, persistent ventricular dysfunction, electrical imbalance, clinical deterioration, and comorbidities should be considered.[22] Routine laboratory tests including troponin level, 12-lead ECG, echocardiography, oxygen saturation, dyspnea, fatigue, muscle strength, physical performance, functional (exercise) capacity, pulmonary function tests, activities of daily living, and health-related QoL should be evaluated in patients with cardiovascular disorders due to COVID-19 disease. Heart rate, blood pressure, oxygen saturation, and clinical symptoms and signs should be recorded at the beginning of the program and at each session of the rehabilitation program.

Evaluation of ECG for arrhythmia, myocardial injury and myocarditis, and chest X-ray for cardiomegaly and COVID-19 pneumonia is

valuable.[23] Although the sensitivity is low, abnormal ECG findings such as frequent or polymorphous premature ventricular beats or arrhythmias, ST and T wave changes, left bundle branch block and atrioventricular block can be seen in myocarditis.[24] It may require monitoring oxygen saturation while walking, activities of daily living and/or during telemetric monitoring.[25]

TABLE 2
Indications of exercise training following cardiac involvement due to COVID-19

1. Ischemic heart diseases
    a. Acute coronary syndrome
    b. Myocardial infarction
    c. Percutaneous revascularization
    d. Coronary artery bypass surgery
    e. Chronic ischemic heart diseases
    f. Stable angina pectoris
2. Compensated heart failure
3. Myocarditis (following the completion of the appropriate rest period)
4. Stress-induced cardiomyopathy (Takotsubo) (following the completion of the appropriate rest period)
5. Arrhythmias
6. Postural tachycardia syndrome
7. Peripheral vascular disease
8. Valvular disease
9. Cardiovascular risk factors
    a. Hypertension
    b. Diabetes mellitus
    c. Metabolic syndrome
    d. Obesity

TABLE 3
Contraindications of exercise training following cardiovascular involvement due to COVID-19

1. Acute phase of COVID-19
2. Other acute infectious conditions
3. Acute myocarditis
4. Acute pericarditis
5. Decompensated heart failure
6. Unstable angina
7. Complex ventricular arrhythmias
8. Arrhythmias causing hemodynamic instability
9. Pulmonary arterial hypertension
10. Intracavitary thrombus
11. Recent thrombophlebitis
12. Acute pulmonary embolism
13. Severe aortic stenosis
14. Uncontrolled systemic conditions such as active rheumatoid arthritis, uncontrolled diabetes, uncontrolled hypertension
15. Musculoskeletal conditions that prohibit physical exercise

To tailor the exercise program, it is necessary to determine the functional capacities of the patients. Particularly, in COVID-19 patients with long-term complications, exercise testing is necessary. The choice of the best exercise test method is ultimately made according to the current condition of the patient and the presence of other problems related to the disease, as well as the existing facilities of the cardiopulmonary rehabilitation units during the pandemic.[26]

Exercise stress test, cardiopulmonary exercise test (CPET) and/or field tests such as the 6-Minute Walk Test (6MWT) is often recommended to determine functional capacity. The CPET may be particularly valuable in athletes presenting with undifferentiated dyspnea or effort intolerance, as it can provide valuable information regarding both cardiac and pulmonary involvement of COVID-19 disease.[26] In addition, exercise test should also be performed in athletes with COVID-19 associated myocarditis after a three- to six-month period of convalescence for return to play risk stratification.[27]

The general indications and contraindications of the exercise test recommended in the guidelines should be followed. There is no indication in the acute phase or in the suspected disease as there is a risk of contaminating the rehabilitation team members by causing aerosol spread. It should be kept in mind that CPET should not be performed in patients with acute myocarditis, since it poses a higher cardiac risk in these patient.[28,29]

Cardiopulmonary exercise test is a tool to identify and to evaluate the severity of cardiopulmonary diseases. Cardiopulmonary exercise test is the gold-standard test in determining functional capacity, and is considered as a vital sign.[30] It is a method that provides valuable clues in *(i)* prognostic and diagnostic value, *(ii)* measuring therapeutic efficacy, *(iii)* determining functional capacity, *(iv)* prescribing exercise.[28] COVID-19 has an impact on functional capacity. About half of COVID-19 survivors have a significant change in predicted peak oxygen uptake (pVO_2) at three months after hospital discharge.[31] Therefore, CPET may give valuable information in patients with or without cardiac involvement. Many CPET laboratories have been suspended due to the increased risk of the COVID-19 pandemic, as resting expiratory flow rates and minute ventilation increase by as much as 10 times during exercise.[32]

Cardiopulmonary exercise test is usually not recommended, particularly in endemic areas where the disease is common. However, testing is required to determine functional capacity in patients with severe HF. Besides, CPET plays an important role in the differential diagnosis of fatigue and dyspnea, as it can identify both cardiac and pulmonary sequelae of COVID-19 disease.[26] Therefore, it is necessary for these laboratories to return to their pre-pandemic practice in terms of monitoring long-term cardiac sequelae.

The functional status of 200 COVID-19 patients discharged between March and November 2020 was evaluated with CPET. The median percent- pVO_2 (pVO_2%) was 88% (78.3-103.1%). In 99 (49.5%) patients, the pVO_2% was found to be below 85%. Of 99 patients with low pVO_2%, 61 (61%) had a normal anaerobic threshold. Among the patients with low pVO_2, 9 (14.8%) respiratory, 21 (34.4%) cardiac and 31 (50.8%) cardiopulmonary causes were found.[31] As a result, there is an increased need for CPET in clinical practice and research due to the cardiac and pulmonary effects of COVID-19 and the symptom of fatigue seen in long-COVID-19. Current clinical guidelines in the United Kingdom recommend evaluation with CPET in clinical trials for long-term COVID-19.[33,34]

When CPET is necessary, prior screening for the symptoms of active COVID-19 (e.g., cough, sore throat, fever, loss of sense of smell and taste) and body temperature checks within 24 h is recommended. Furthermore, infection should be ruled out by performing a polymerase chain reaction (PCR) SARS-CoV-2 test within 48 to 72 h of CPET.[18,35] The use of viral filters is recommended for some CPET devices. However, it should be noted that test results may be affected.[35]

The 6MWT is the most widely used field test to assess cardiopulmonary capacity. It was primarily designed for use in adults with chronic respiratory disease;[36,37] therefore, it was used in COVID-19 patients with or without pulmonary involvement. Since the relationship between the distance walked and the peak oxygen uptake in the CPET was found to be moderate to strong,[37] it is also a suitable method to determine exercise capacity in patients with cardiac involvement.

Traditionally, the 6MWT is performed without a face mask. The use of mask is thought to affect performance. In a study, it was found that the mean difference in 6MWT distance was 65 m when using a surgical or N95 face mask, compared to not wearing a face mask.[38] However, another study suggested that surgical or N95-type face masks may be used during 6MWT, particularly among those recovering from

COVID-19. According to the study, oxygen saturation (SpO_2), heart rate, and degree of shortness of breath, as well as walking distance, were similar to those without a face mask.[39]

Mantha et al.[39] suggested some modifications of the 6MWT, such as using a continuous finger pulse oximeter for SpO_2 monitoring and wearing a surgical mask in laboratory-confirmed adult patients with uncomplicated or mild illness due to the characteristics of COVID-19. They also reported that the availability of the 100-foot track is not mandatory, as the total distance walked is important. Suggested modifications are listed below:

- Performing on the fourth or fifth day of clinical illness
- Wearing a surgical mask
- Single cut-off for distance walked <0.26 miles (<1400 feet or 420 meters) or less than 90% SpO_2,
- Contraindicated for testing if SpO_2 is ≤93% in room air, at rest
- The presence of a physician is mandatory
- Evaluation of dyspnea and fatigue is mandatory
- Stop testing when saturation drops below 90%.

Body function and structure of the patients should be assessed in detail before and after rehabilitation. These assessments demonstrate the impact of the disease and assess mental and physical suitability of the patient to the planned rehabilitation protocols. Muscle strength and mass, fatigue, pain, shortness of breath, balance, level of physical function, and frailty should be evaluated. For these purposes, anthropometric measurements, body composition analysis, range of motion in the joints, radiological examinations, Medical Research Council Sum Score, handgrip power (e.g., by using hand dynamometer), the one-repetition maximum (1RM) test, measurement of maximal inspiratory and expiratory pressure (MIP, MEP), Fatigue Severity Scale, Visual Analog Scale (to evaluate pain or dyspnea), Medical Research Council Dyspnea Score, endurance testing (e.g., push-up test), walking speed, walking distance, Short Physical Performance Battery, static and dynamic balance measurements can be used. Moreover, in several studies clinical measures have been used for the assessment of frailty in COVID-19 patients such as the FRAIL scale, Frailty Index, and Clinical Frailty Scale. During the COVID-19 pandemic, the frequency of frailty has increased in the elderly population. Furthermore, individuals with COVID-19 also have an increased risk of frailty. Physical impairments are associated with reduced QoL, particularly perceived role-physical. Similarly, the number of chair raises in the one-minute sit-to-stand test was associated with reduced quadriceps and biceps strength in remitting COVID-19 patients. Clinical frailty scale was shown to be predictive for comorbidity, mortality, complications, length of hospital stay, falls, poor cognition, and functional dependence in COVID-19 patients.[40-45]

Prolonged physical symptoms after COVID-19 disease, including cardiovascular involvement, are closely associated with a higher probability of developing psychiatric illness. Sleep disorders, depression, anxiety, somatic symptoms, panic attacks, psychosis and post-traumatic stress disorder are reported in these patient groups. Furthermore, depression is reported to double its prevalence during the COVID-19 pandemic in patients with cardiovascular disease. In patients with psychiatric problems, problem-specific standard assessment tools are used. The Hospital Anxiety and Depression Scale, Beck Depression Inventory, and Beck Anxiety Inventory are among the most frequently used scales. Additionally, mental functions can be evaluated using the Mini-Mental Test.[43,46]

The New York Heart Association (NYHA) classification provides a general functional classification in HF. Similarly, the functional limitation of an individual with COVID-19 can be evaluated with the Post-COVID-19 Functional Status Scale.[40] For PA, the International Physical Activity Questionnaire, the Physical Activity Scale for the Elderly can be used. Activities of daily living can be evaluated with scales such as Barthel Index, the EQ-5D-5L.[47] It is also important to evaluate the QoL of patients. Some of the most commonly used generic scales for the assessment of health-related QoL are the Short Form-36 (SF-36), the SF-12 and the EQ-5D. Many different clinics may occur in patients with cardiac involvement due to COVID-19. Therefore, it can be evaluated with disease-specific QoL scales according to the cardiac problem due to COVID-19. The Turkish validity and reliability studies were conducted for some of these disease specific scales. Most emphasize symptoms referable to the given disease, physical functional limitations related to those symptoms, and questions about well-being/QoL. There are no standard criteria in choosing one of these instruments over another. The choice is driven often in accordance with the primary disease of interest (such as coronary artery

disease or HF). Frequently, generic and disease-specific health status surveys are used simultaneously in studies.[48] There is not enough data related to the effects of CR to QoL in different cardiac presentation caused by COVID-19 in the literature. However, it has been reported that low physical function and fatigue are usually associated with low QoL in COVID-19 patients, and also has been reported that rehabilitation effects the QoL positively.[41,44,45] Comprehensive assessment of all aspects of health is an important step in formulating an individualized treatment plan focused on returning to social life.[47]

TIMING OF CARDIAC REHABILITATION FOR COVID-19 PATIENTS WITH CARDIAC INVOLVEMENT

There is no consensus regarding the timing of CR in COVID-19 patients with an underlying heart disease and/or have cardiovascular problems as a complication of the COVID-19 disease. However, it is usually considered appropriate to start CR from the fourth week after the illness.

Delphi consensus by 28 experts from the European Association of Preventive Cardiology (EAPC) provides recommendations on timing of the CR in COVID-19 patients with concerns about starting rehabilitation during the acute phase of the disease.[49] While prescribing the exercise component of the CR in COVID-19 patients, the stage of the disease should be taken into account.[49,50]

For confirmed cases of myocarditis, avoiding exercise programs for a period of three to six months is recommended to ensure biological and clinical resolution of the cardiac dysfunction.[1,51] In case of pericarditis without myocarditis, resuming an exercise program can be considered after six weeks of acute phase.[1] If there is unstable HF, admission to the CR should be delayed.[1,52]

In patients with severe ventricular arrhythmia/tachycardia that persists in the post-acute period, CR programs should definitely be monitored and aerobic exercises such as running and walking as part of CR program may need to be delayed.[51,52]

CARDIAC REHABILITATION SERVICE SETTINGS FOR POST-COVID-19 PATIENTS

For COVID-19 patients, an integrated rehabilitative process is recommended, involving a multidisciplinary and multi-professional team providing neuromuscular, cardiac, respiratory, and swallowing interventions, and psychological support, to improve patients' QoL. In studies, the effectiveness of CR has also been shown in patients with post COVID-19 cardiac involvement.[51,53,54]

Various rehabilitation modalities have been used during the COVID-19 pandemic, including hybrid models that are likely to be offered as an alternative to hospital-based rehabilitation in the future. It is anticipated that these new approaches would increase patient selection and participation in CR. While participation in conventional hospital-based outpatient and inpatient CR programs has declined, the proportion of patients receiving home-based rehabilitation in the United Kingdom has increased by more than three-fold since the pandemic.[55]

Cardiac rehabilitation programs are designed according to risk levels (highest risk, medium risk, lowest risk), it is similar for post COVID-19 cardiac involved patients, in both hospital and home settings.[51,53] Although the risk of adverse events during CR for in post-COVID-19 patients is low, Center-Based CR (CBCR) can be preferred if the following conditions exist: saturation <88 to 93%, heart rate <40 bpm, or >120 bpm, systolic blood pressure <90 mmHg or >180 mmHg, body temperature fluctuations >37.2°C, respiratory symptoms and fatigue that worsen during exercise and are not alleviated with rest, symptoms such as chest tightness or pain, difficulty in breathing, severe cough, dizziness, headache, unclear vision, palpitations, sweating and instability.[51] Prognostic implications of troponin elevation, and indications for cardiac MRI in diagnosis and management is important. Cardiac MRI with late gadolinium enhancement can identify the functional capacity of the at-risk group and is also associated with prognosis in patients with heart disease. This method is a better predictor of outcome than diagnostic testing alone. The late risk of arrhythmias in patients is currently unknown and perhaps Holter or telemetry monitoring during CR may be prudent at a facility.

The finding of myocarditis as a significant cause of sudden death in the young is notable and relevant to survivors of COVID-19. Post-COVID-19 athletes with myocardial injury who had abnormal ECG, are advised to restrict sports activities for three to six months and, when they recover from severe illness, they should be hospital based for CR.[56]

Patients with COVID-19 who have severe peripheral edema accompanying to HF or severe HF such as NYHA Class III-IV are contraindicated

for rehabilitation and may be hospitalized to be compensated for CR. The European Society of Cardiology HF guideline recommends the use of telephone and remote monitoring in the management and follow-up of HF patients at home. Non-invasive and/or implantable devices can be used for monitorization, as well. Telemonitoring is useful to improve patient care, to reduce frequency of clinical visits and to reduce costs to healthcare services in HF patients.[57]

Telerehabilitation that consists of the use of video calls or properly structured platforms may be useful as an alternative treatment choice. Remote CR is safe and effective as well in post-COVID-19 patients with cardiovascular disease but monitoring systems that supply for oximetry, blood pressure control and ECG follow-up are needed, particularly in the management of complicated patients.[51]

Home-Based CR (HBCR) has similar effectiveness as CBCR. COVID-19 has negative effects on the traditional facility-based CR model. It may be a reasonable alternative treatment. As COVID-19 pandemic continues, cardiovascular providers continue to seek novel technologies by defining and monitoring patient and CR program outcomes, organize the technology to enhance care delivery, and finally develop a hybrid CR model to facilitate the restrictions due to being physically distant.[51] Currently, promising experiences are reported in the literature related to the use of telerehabilitation for a big number of patients with a favorable cost/effectiveness ratio in CR. Remote cardiorehabilitation is also found safe and effective for cardiovascular disease or post-cardiac surgery patients. For these patients, a hybrid treatment may be suitable, limiting the existing rehabilitation to minimum, preferring the remote modality, follow-up with periodic evaluations and treatments in-presence.[51]

GENERAL RECOMMENDATIONS BEFORE STARTING EXERCISE TRAINING

These are listed as follows:

- The patient and his/her family should be educated on the clinical features and its treatment, comorbidities, long-term potential consequences of the disease, the purpose and effects of rehabilitation, hygiene, sleep, and proper nutrition.[53,58-60]
- COVID-19 disease can cause multisystem involvement and serious complications and, therefore, the patient should be re-evaluated, closely monitored and followed during rehabilitation practices against the possibility of deterioration in clinical status.[59,61,62]
- Other clinical conditions such as neurological and respiratory conditions that would affect exercise prescription should be carefully evaluated before CR. Anxiety and depression in the acute period, post-traumatic symptoms and post-traumatic stress disorder in the chronic period can be encountered. Psychosocial evaluation should be performed before the program and treatment approaches should be provided when necessary.
- These patients have many problems due to their previous diseases, long stays in the hospital or ICU, and complications from COVID-19. These multiple problems, which can start during hospitalization and continue after discharge, create a need for new regulations in the implementation of classical CR programs.
- General rehabilitation practices should be continued in parallel with CR for other problems such as neurological, respiratory, musculoskeletal, cognitive disorders, speech and swallowing problems, and other problems related to immobilization.
- It should be kept in mind that there is a possibility of recurrent COVID-19 infection; therefore, the patient should be questioned for symptoms during post COVID-19 rehabilitation.[63,64]

THE IMPORTANCE OF EXERCISE IN POST COVID-19 PATIENTS DURING CARDIAC REHABILITATION

Regular PA supports the immune system, protects against respiratory diseases and COVID-19. With exercise, the inflammatory response and stress hormones decreases; and the lymphocytes, natural killer (NK) cells, immune B cells and monocytes increases. Thus, immunovigilance improves and the systemic inflammatory response decreases.[65,66]

The frequency, intensity and duration of exercise affects the immunomodulatory response. Regular exercise reduces mortality in pneumonia and influenza infection, restores cardiorespiratory function, improves endothelial dysfunction, increases vaccine response; regulates lipid, glucose and insulin

metabolism.[67-69] Regular moderate exercise is recommended, as high-intensity exercise at a level higher than present physical fitness can suppress immunity and increase the risk of subclinical viral infection.[70] High-intensity, prolonged (more than 90 min) exercise with insufficient rest time; disrupts cellular immunity, predisposing to infection.[64]

In patients with post-COVID-19 syndrome, regardless of their previous comorbid conditions, a decrease in fatty beta acid oxidation and an increase in lactic acid accumulation during exercise were detected.[71]

Insufficient mitochondrial response to exercise should be considered in patients with post-acute COVID-19 syndrome without cardiopulmonary sequelae. In the presence of a previous COVID-19 infection, even without any cardiopulmonary sequelae, the patient may have a decrease in peak aerobic exercise capacity, impaired systemic oxygen extraction, and an exaggerated hyperventilation response to exercise.[66]

Considering these physiological responses, it is recommended to keep warm-up and cooling periods longer, when planning an exercise prescription for CR. Total exercise time should be extended more slowly, considering that, there may be an accumulation of lactic acid earlier than normal, and the intensity of exercise should also be more slowly increased than routine CR regimens.

EXERCISE COMPONENT IN CARDIAC REHABILITATION

- Exercise training, the cornerstone of CR, should be applied together with other components of CR.
- A good understanding of the cardiovascular system involvement due to COVID-19 is of utmost importance in terms of the starting time of the CR program, the duration, type, intensity of the exercises, the grade of supervision and monitoring during the program, the termination criteria and the setting of the program.
- Low-grade cardiac injury after COVID-19 may be present and should be kept in mind to avoid vigorous exercise or work-out.[72]
- In those with pre-existing cardiovascular disease, exercise program should be re-arranged by considering other problems in the post COVID-19 period.

Types of exercises in cardiac rehabilitation

The main types of exercises in the CR program are aerobic, strengthening and flexibility exercises (Table 4). However, depending on the type of cardiac involvement, breathing exercises, balance-coordination exercises, relaxation exercises can also be added to this program.[72,73]

Aerobic (endurance) training:

- Baseline symptom-limited CPET using a treadmill or bicycle is the gold standard to determine the intensity of aerobic exercise and to detect possible risks during exercise training. If this test cannot be performed, 6MWT or incremental shuttle walk test (ISWT) may be used. Short physical performance battery or other chair-based tests can be used in patients who are very weak, frail, or unable to walk. In patients whose aerobic exercise intensity cannot be determined by objective methods for any reason, subjective tests such as Borg rating of perceived exertion scale (RPE) or talk test can be used.[73,74] Aerobic exercise intensity method such as "Resting Heart Rate +20–30 bpm" and RPE "11-14" can also be used in patients without baseline stress test in the post-COVID-19 period. The patient should be followed very closely in terms of "new symptoms with exercise training".[75]
- Before starting aerobic exercise training in post-COVID-19, detailed medical history, physical examination and laboratory findings should be evaluated together and an individualized exercise program should be planned according to the needs of the patient.
- In particular, supervised programs are recommended at the beginning to monitor exercise tolerance and individual responses, to confirm clinical stability and to identify signs and symptoms that indicate changing or terminating the program. This period depends on the characteristics of the post-COVID-19 patient. Supervision should include monitoring of symptom and signs, heart rate, blood pressure, and rhythm before, during, and after exercise training. The period of supervision should be extended in patients with new symptoms and signs, blood pressure abnormalities, and increased supraventricular or ventricular ectopia

TABLE 4
Aerobic and resistance exercises in Cardiac Rehabilitation Program after COVID-19

Aerobic exercises*	
Determining method of exercise intensity	***Objective methods*** • Cardiopulmonary exercise test • 6-min walk test • Incremental shuttle walk test • Short physical performance battery ***Subjective methods*** • Borg rating of perceived exertion scale (BORG RPE) (RPE "11–14" • Talk test • Resting Heart Rate +"20–30"
Supervision need during exercise	• Close monitoring and supervision needed during cardiac rehabilitation sessions especially at the beginning of the program and high risk patients. • Duration of supervision is planned due to observed symptoms and findings during exercise • Monitoring of symptoms and signs, heart rate, blood pressure, rhythm, oxygen saturation before, during, and after exercise training
Training method	***Continuous training*** • Start low to moderate intensity (40% VO_2 peak or HRR, 50% HR peak or WR peak) • 5-10 min of warm-up, 20 min of exercise, 5-10 min of cool down • Borg rating of perceived exertion scale "12-13" • 3-5 times/week ***Interval training*** • Low intensity interval training: low intensity (2-3 MET) period followed by complete rest (passive interval) • 20 min exercises, 3-5 times/week • High Intensity Interval Training should be preferred in selected patients or advanced stages of program
Strength exercises*	
Determining method of exercise intensity	• 1 repetitive maximum method • Adult Omnibus Resistance Exercise Scale (OMNI-RES)
Supervision need during exercise	• Close monitoring and supervision needed during cardiac rehabilitation sessions especially at the beginning of the program and high risk patients. • Duration of supervision is planned due to observed symptoms and findings during exercise • Physical examination, monitoring of heart rate, blood pressure, rhythm, oxygen saturation before, during, and after exercise training
Training method	• Upper extremities at 30-70% of 1 RM • Lower extremities with 40-80% of 1 RM • 2-4 seconds for concentric and eccentric phase • 8-10 muscles selected from upper and lower extremities • 2-3 sets; 8-12 repetitions/set for each muscle group

* See the relevant section in the text for exercise prescribing in special groups.

during exercise.

- Some patients without hypoxemia at rest or patients with concomitant pulmonary disease may show marked arterial oxygen desaturation and hypoxemia during exercise. Although a flow of 1-2 L/min is sufficient during ambulation in patients receiving continuous oxygen at rest, it is appropriate to increase this amount by 1 L/min in exercise training during CR.
- Continuous or interval aerobic exercise training can be used depending on the evaluation of the post-COVID-19 patient.
- In accordance with the general CR principles, in post-COVID-19 patients with moderate-to-good exercise tolerance, aerobic continuous training can be started with low to moderate exercise intensity (40% VO2peak or HRR, 50%

HR peak or WR peak) and at least 20 min of exercise after a 5 to 10-min warm-up period. The exercise session lasts with a 5 to 10-min cool-down period. Borg RPE scale should be "12-13" and exercise frequency should be 3 to 5 times a week. As exercise tolerance increases, exercise-related parameters can be rearranged.[51,74,76,77]

- Interval aerobic exercise training is preferred for those who cannot perform continuous aerobic exercise for a long time due to various reasons, particularly in elderly, frail, weak patients and those with severe exercise dyspnea. Low-intensity (2-3 METs) aerobic training is followed by periods of complete rest (passive interval). Active exercise time should be at least 20 min and should be performed be 3 to 5 times a week. It should be considered that interval training would be better tolerated than continuous aerobic training in weak and frail patients whose fatigue symptoms continue after COVID-19.[51,74,76]
- It is thought that the cardiovascular benefits of "High Intensity Interval Training" (HIIT)" is another interval aerobic exercise training method, are greater than aerobic continuous and passive interval aerobic training method. In this training method, high-intensity aerobic exercise is performed consecutively with active interval periods of low-intensity aerobic exercise. The risk of acute cardiac events was found to be six times higher than that of moderate-intensity continuous aerobic exercise training programs.[51,73,76] Extreme fatigue and respiratory distress are other complications. Particularly, in the early post-COVID-19 period, mild to moderate continuous training programs or passive interval training program should be considered as a more appropriate aerobic exercise training method. The HIIT should be prescribed in selected patients who are stable and in advanced stages of the CR program.

Strength training:

- It should be kept in mind that strength exercises would lead to significant increases in blood pressure and heart rate, and then decreases in blood pressure that can last 24 h after exercise.[78,79]
- The intensity of strength exercise for post-COVID-19 patients is determined by using the 1RM method, as in classical CR programs. The 1RM method is safe in patients with mild to moderate left ventricular dysfunction. However, the intensity can be determined by using subjective methods such as Adult Omnibus Resistance Exercise Scale (OMNI-RES) in post-COVID-19 patients who are very weak, frail and have multiple systemic problems.[73,74]
- In-post COVID-19 patients with moderate-to-good exercise tolerance, strength exercises can be started with moderate intensity (for the upper extremities at 30 to 70% of 1RM and for the lower extremities with 40 to 80% of 1RM) at 8 to 10 muscles selected from the upper and lower extremities and applied to each muscle group with 2 to 3 sets. Each set should be 8 to 12 repetitions with 2 to 3 min rest between sets and 2 to 3 times a week. Large muscle groups or muscle groups used during daily living activities are preferred.[51,73,74,77] Each movement should be slow and the concentric phase and the eccentric phase should last 2 to 4 sec in total. Weights should be lifted without causing pain and discomfort. Valsalva maneuver should not be created by exhaling while lifting. As the resistance exercises may increase the cardiovascular event risk in cardiac patients, first session of the patients must be applied under supervision and monitorization in rehabilitation facilities that are specifically designed and equipped for these emergencies. The period of supervision should be extended according the characteristics of the post-COVID-19 patient.[73,74]

Exercise training in special groups

- The program should be started under supervision and monitoring in post-COVID-19 patients who are over 75 years old, weak, frail and have multiple systemic problems. In these patients, it is often impossible to perform a baseline exercise test to determine aerobic exercise intensity. Exercise training can be started 2 to 3 times a week with a heart rate slightly below the heart rate achieved in the 6MWT. Aerobic exercise intensity method such as "Resting Heart Rate +20 to 30 bpm" and RPE "11-14" can also be used if any baseline stress test could not be performed. Neuromuscular electrical stimulation (NMES) method or continuous aerobic training with low-moderate

exercise intensity or low-intensity passive interval aerobic training methods can be used for exercise program. The safety of exercise training is ensured by Borg RPE scale and talk test. Strength exercises can be started with 6 to 8 muscles selected in the upper and lower extremities, an intensity of less than 30% of 1 RM, Borg RPE scale 11-12, and 5 to 8 repetitions for each muscle. It is gradually increased to 40 to 60% of 1RM, Borg RPE scale >15 and 8 to 15 repetitions. Appropriate rest should be given between sets. The program is progressed step by step by training selected muscles. Exercise training should also have a balance-training component.[53,73,75-77]

- In post-COVID-19 patients with HF, strength exercise, inspiratory muscle training and NMES training can also be used in addition to continuous or passive interval aerobic exercise training.[73]
- Patients receiving exercise training during pulmonary or CR after COVID-19 should be carefully observed for the symptoms of myocarditis. Those symptoms are reported as mild symptoms like fatigue, dyspnea or chest pain/pressure, chest tightness, dizziness, syncope on exertion. Some patient may show tachycardia, acute onset of HF and cardiogenic shock. Fulminant myocarditis may present with low pulse pressure, tachycardia and decreased temperature and color change in lower extremities.[11] International guidelines are followed in patients with myocarditis or cardiomyopathy due to COVID-19 and exercise training should not be started for three to six months. Exercise training can be initiated, if left ventricular function and myocardial injury biomarkers are normal and there is no relevant arrhythmia in the 24-h ECG monitoring and exercise testing. However, these patients should be reassessed periodically, particularly during the first two years.[53,80] Electrocardiography may also be observed at the initial sessions of program for the ECG findings of myocarditis.[11]
- New-onset autonomic disorders such as POTS, orthostatic hypotension and neurocardiogenic syncope can be seen after COVID -19 infection.[81-83] It should be kept in mind that autonomic dysfunction may develop even after asymptomatic COVID-19 infection. Postural orthostatic tachycardia syndrome is one of the most common autonomic disorders with a wide range of clinical manifestations which is usually seen after bacterial and viral infections and the symptoms may last six to eight months.[83]

Some non-pharmacological treatment approaches such as increasing fluid and salt intake, using high-waisted compression stockings or abdominal binder, exercising in the sitting or supine position (recumbent bicycle or rowing) can be attempted at the beginning of CR sessions in post-COVID-19 patients with autonomic dysfunction. Exercises in the standing position (walking, elliptical machine) should be started after a tolerance is obtained to the sitting or supine position exercises.[83,84] If these preventive measures are not sufficient, pharmacological approaches such as beta-blockers, fludrocortisone, midodrine, ivabradine may be added to the treatment.[83]

Exclusion and exercise termination criteria

Exercise training should not be started in the presence of the following criteria or intervention should be terminated in case of significant deterioration:[51,58-62]

1. Body temperature fluctuations above 37.2°C
2. Respiratory symptoms that worsen during exercise and are not relieved after rest or BORG dyspnea score >4 during low intensity exercise.
3. Heart rate <40 or >120 bpm
4. Resting heart rate should not increase more than 20 bpm during low intensity exercise.
5. Blood pressure <90/60 or >180/90 mmHg
6. Oxygen saturation should be maintained above 90%. Care should be taken to ensure that the oxygen saturation does not fall more than 4 to 5% and not below 88% for a period of half to 5 min.
7. Fatigue that worsen during exercise and are not relieved after rest or the BORG RPE score >11-12 during low intensity exercise.
8. The presence of general contraindications for exercise training such as angina pectoris, recent MI, severe pulmonary hypertension, decompensated HF, complex arrhythmia, deep vein thrombosis or pulmonary embolism, unstable diabetes, hepatic, renal or neurological disorders, inability to perform exercise due to musculoskeletal difficulties, and cognitive

dysfunction or altered consciousness.

9. Worsening of clinical status and appearance of symptoms such as chest tightness or pain, difficulty in breathing, severe cough, dizziness, headache, unclear vision, palpitations, sweating and instability. Inability to follow exercise program and commands due to the impaired consciousness or irritability

CONTAGION PRECAUTIONS, CLEANING OF USED TOOLS

A collaborative approach should be adopted in the conduct of hospital-based CR programs during the COVID-19 era, involving administration, the infection prevention and control department, medical director and staff. It should be noted that there is a need for continuous adaptation and updating of planning and methods for CR practices throughout the pandemic, taking into account current COVID-19 outbreak management guidelines. In various guidelines, it is recommended that at least four-week interval from diagnosis for the initiation of CR programs in patients with COVID-19, but changes in the transmission characteristics of COVID-19 over time and pre-program COVID-19 test results of patients should be considered in the timing of rehabilitation.[85,86] Patients and staff should be evaluated daily for sign or symptoms associated with COVID-19 and the current isolation protocols should be followed for patients and staff who have positive COVID-19 test. Patients should be educated on hand hygiene, correct use of face masks, and coughing. It should be considered that wearing a mask during exercise may reduce the patient's exercise tolerance and may require some adjustments in exercise prescriptions. Precautions for reducing the risk of contamination during exercise include maximizing distance between patients, staff, and equipment, using appropriate personal protective equipment and sufficient air exchange. According to the recommendations of the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR), staff should maintain 6 feet (1.8 meters) social distancing as much as possible with patients.[85] In the Guidance to COVID-19 Infection Control Measures and Working in the Healthcare Institutions published by the Republic of Türkiye, Ministry of Health, it is proposed that the distance between staff and patient be at least 1 meter.[86] In general, the recommended distance between equipment is at least 6 to 12 feet (1.8-3.7 meters). Equipment and frequently touched surfaces should be thoroughly disinfected between each patient using a hospital-approved disinfectant. In addition, remote and home-based treatments may be considered for eligible patients for reducing the risk of contamination.[85,86]

PHYSICAL ACTIVITY RECOMMENDATIONS FOR PATIENTS WITH CARDIAC INVOLVEMENT DUE TO COVID-19

Physical activity may be a key component of long-term recovery from COVID-19 and it has prominent physical and mental health benefits especially after a period of limited PA due to restrictions. Furthermore, meeting PA guidelines was strongly associated with a reduced risk for severe COVID-19 outcomes among infected adults.[87] However, patients recovering from COVID-19 with cardiovascular complications require guidance and necessary precautions should be taken into consideration through a gradual return to activity. Up to date, there are no definitive evidence-based guidelines for PA recommendations for these patients; all current guidance to date is based on consensus or expert opinion. It is recommended that patients with mild or moderate disease and who have no cardiac symptoms may return to their previous level of PA gradually after symptom-free 7 to 10 days; first preforming routine daily activities such as going to work, doing daily chores, secondly performing light PA activities such as walking, and lastly, gradually returning to sports/PA activities.[88,89] If symptoms such as palpitation, chest pain or dyspnea occur, patient should be evaluated medically. Any finding suggestive of cardiac injury should prompt strict limits on activity (no more than a brisk walk). Most of the expert reviews on the PA recommendations after cardiovascular involvement is about the timing of return-to-play in athletes, yet, these recommendations may be carried out for other patients having similar conditions, as well. Gluckman et al.[1] recommends that athletes recovering from COVID-19, but still having cardiopulmonary symptoms (chest pain/tightness, palpitations, or syncope) and/or those requiring hospitalization for cardiac involvement are recommended to be further tested by ECG, cardiac troponin, and echocardiogram. These tests should also be performed in individuals who develop new cardiopulmonary symptoms after return to PA or exercise. The English and Scottish Institute of Sport guidance suggests that before re-initiation of sport for athletes, activities of daily living should be easily achievable and the person should be able to walk 500 meters on the flat without feeling excessive fatigue

or breathlessness.[89] Individuals with myocarditis should abstain from exercise for three to six months, but there is no further recommendation about the level of PA. Maximal exercise testing is not recommended in case of myocarditis. These patients may perform their daily living activities and brisk walking to the extent to which symptoms allow. In case of COVID-19-related pericarditis, current recommendations specific to exercise restrictions are consistent with the recommendations for other etiologies of pericarditis.[90,91] Currently, the European Sport Cardiology Section of the European Association of Preventive Cardiology (ESC/EAPC) and AHA/ACC guidelines recommend that individuals with active pericarditis and/or myocarditis should avoid exercise and should return to exercise after complete recovery.[90,91] Individuals may start all types of exercise including competitive sports after 30 days to three months depending on clinical severity after resolution of active disease clinically, and demonstrated by echocardiography and serum markers.

In conclusion, there is no clear, evidence-based guidelines for PA recommendations for patients with COVID-19 related cardiovascular involvement. Yet, based on the general measures related to other cardiovascular disease, especially after other viral diseases or unknown etiology, PA recommendations should be individualized and based on the subjective compliance and symptoms. Patients may start with breathing and gentle flexibility exercises and gentle walking not exceeding a RPE of 6 to 8.[92] In case no symptoms occur, patients may progress to low intensity walking, light yoga or light household/gardening activities within a RPE of 6 to 11 after seven days. Duration of PA may be 10 to 15 min and gradually increased to 30 min. Further increase in duration and intensity of PA should be done in accordance with the CR guidelines and exercise restrictions for this group of patients.

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