

REVIEW ARTICLE

Stress and Physical Inactivity: Two Explosive Ingredients for the Heart in COVID-19 Pandemic Times

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Abstract: Background: Coronavirus disease 2019 (Covid-19) pandemic is a global health crisis that has culminated in thousands of deaths. In order to reduce the spread of the Sars-CoV-2 virus, governments of several countries have adopted social isolation as a strategy. However, social isolation has culminated in deleterious effects on the population's health, including increased physical inactivity, stress and, consequently, adverse changes in body composition, cardiorespiratory capacity, muscle strength, physical functionality, and vascular events, which are increasingly pointed out as the main determinants of cardiovascular health. Staying physically active during lockdown is a challenge, especially for the population with a higher risk of mortality from COVID-19, who are still encouraged to maintain social distance until there is a vaccine available. Strategies to avoid physical inactivity and reduce stress levels can promote cardiovascular protection and must be considered during COVID-19 time.

Objective: The aim of this paper is to discuss the risks of physical inactivity and stress for the cardiovascular system during the COVID-19 pandemic and propose strategies to protect cardiovascular health.

Conclusion: A home-based training protocol could be an interesting and effective strategy for the population who need to remain physically active and safe at home.

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1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic is a globally impacting health crisis that has resulted in high mortality and morbidity [1]. To date (November 15, 2020), over 53.7 million cases have been reported, and more than 1.3 million deaths have been confirmed [2] worldwide. Among the effective strategies to minimize contagion, social isolation has been found as one of the main ways to decrease viral spread [3]. However, prolonged quarantine may result in unfavorable sedentary behavior (*i.e.*, physical inactivity, 'too much sitting' behavior and energy expenditure of ≤ 1.5 metabolic equivalent method - METs [4]) and chronic stress, increasing the risk of chronic disease [5]. In fact, recent studies have already pointed out potential risks related to physical inactivity and social isolation [6-12]. Physical inactivity and sedentary behavior are associated with adverse changes in body composition, cardiorespiratory capacity, muscle strength, physical functionality, and vascular events

[13], which are increasingly pointed out as the main determinants of cardiovascular health [14]. Especially in elderly individuals, physical inactivity results in increased age-related muscle waste, accelerating the progression of sarcopenia and associated comorbidities [11]. Chronic stress is also associated with the development of cardiovascular diseases [15], with the stress-related reduction in the physical activity being an important factor for cardiovascular risk. In addition, the long-term development of an atherosclerotic process and subclinical coronary heart disease also occur with stress and acute exposure to stress can trigger cardiac events in people with advanced coronary heart disease [15]. Stress can also affect the autonomic nervous system, decreasing heart rate variability, thus increasing the cardiovascular risk [16]. In Brazil, a study assessed the changes in the habits of the participants engaged in physical activities in relation to their practices due to the social distancing during the COVID-19 period. Importantly, 79.4% of the participants reported that the quarantine had an impact on their physical activities, and many had to interrupt or decrease the frequency of physical activity. Participants who felt a higher impact of social isolation on physical activity tended to show symptoms of anxiety, depression and poor mental health [17].

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Recommendations for the social isolation period include maintaining physical activity and avoid prolonged periods of time spent sitting. Therefore, strategies to avoid physical inactivity and reduce stress levels can promote cardiovascular protection, and must be considered during COVID-19 time [18]. This paper aims to discuss the risks of physical inactivity and stress during the COVID-19 pandemic for the cardiovascular system and to propose strategies to protect cardiovascular health.

2. IMPACT OF PHYSICAL INACTIVITY ON CARDIOVASCULAR HEALTH

Data from the World Health Organization indicate that 31% of individuals over 15 years of age are physically inactive [19]. Even short periods of reduced physical activity can result in deleterious effects in many biological systems [7]. Sedentary behavior leads to a positive energy balance resulting in a fat deposition which is related to systemic inflammation [19], favoring the prevalence of obesity and type 2 diabetes. A recent study found that even short-term changes in physical activity and sedentary behavior in response to COVID-19 restrictions can become permanent, leading to an increased risk of obesity, diabetes and cardiovascular disease in children living in the United States [12]. Another study carried out in Italy showed that the lockdown culminated in a lower rate of physical activity and was correlated with significantly higher weight gain in obese individuals [20]. This scenario increases the risk of mortality from COVID-19 and cardiovascular diseases [21]. It is estimated that 3.2 million deaths per year are related to physical inactivity [22]. In parallel, individuals with cardiovascular diseases may present the most severe symptoms of COVID-19 [18]. Thus, a significant concern arises with the deleterious effects of physical inactivity on the cardiovascular system during the COVID-19 era [23].

Cardiovascular disease is the leading cause of death worldwide, reaching around 17.9 million deaths each year. Much of the burden and mortality from cardiovascular disease is related to unhealthy behaviors, including physical inactivity and low cardiorespiratory capacity [24]. A sedentary lifestyle usually results in increased inflammation associated with atrial fibrillation [25], visceral adiposity, sarcopenia, atherogenic dyslipidemia, arterial hypertension, endothelial dysfunction, type 2 diabetes, and insulin resistance [14]. For instance, reduced VO₂ max and muscle volume are evident after two weeks of bed [26] rest. It is essential to highlight that a reduction of 1 MET in VO₂ max is associated with an 18% increase in cardiovascular disease incidence [27, 28], and the vast majority of these risk factors (*i.e.*, arterial hypertension, type 2 diabetes, visceral adiposity) also imply the severity of the COVID-19 symptoms [29].

Another relevant impact of a sedentary lifestyle occurs on the autonomic nervous system (ANS) control [30]. ANS is responsible for controlling all parts of the body, except skeletal muscles. Through ANS, the physiological integrity of cells, tissues, and organs is maintained, ensuring body homeostasis [31]. Importantly, ANS is the main regulator of

circulatory adjustments in the face of acute hemodynamic changes [32]. The nerves in the carotid sinus are responsible for detecting changes in blood pressure and humoral factors, triggering sympathetic and parasympathetic autonomic reflexes [32, 33]. These nerves influence cardiovascular homeostasis in two main ways: inhibiting the sympathetic impulse through their activation, which prevents an increase in blood pressure, or increasing sympathetic activity when blood pressure decreases [32]. Consequently, autonomic imbalance might be related to vascular diseases and culminates in target organ damage, cardiovascular events, and aggravate disability deficits [34].

In particular, impairment in autonomic control is associated with the onset of hypertension, and hypertensive patients are more predisposed to cardiovascular events and stroke than individuals with normal blood pressure [35]. In this sense, stroke patients usually present decreased heart rate variability, autonomic imbalance, and impaired cardiac vagal modulation [34]. The onset and progression of stroke can be determined by afferent and efferent vagal pathways, especially by central and peripheral inflammation, which may either lead to stroke or be stroke-induced [34, 36]. Considering that arterial hypertension and vascular injuries are important causes of morbidity and mortality due to COVID-19 [18], controlling blood pressure, and managing damage to organs is crucial to reduce this risk [35].

It is worth mentioning that muscle inactivity can result in a condition in the legs called deep vein thrombosis [37]. Pulmonary embolism is commonly a consequence of deep vein thrombosis and it is associated with greater mortality [38]. This risk must be taken into account, especially by patients with COVID-19 who must remain in isolation [39]. A form of diagnosis of venous thromboembolism is the investigation of D-dimer levels (*i.e.*, a breakdown product of soluble fibrin that results from the ordered breakdown of thrombi by the fibrinolytic system) [40]. Interestingly, a recent meta-analysis found that mean D-dimer levels, were significantly increased in patients with severe COVID-19 infection. This evidence suggests that patients with COVID-19 presenting elevated D-dimer levels have an elevated risk of mortality [39].

Sedentary behavior is also related to increased inflammation [14], which is associated with ANS [41]. Studies have further strengthened the hypothesis of a direct relationship between ANS and immune responses. Pieces of evidence show that the cholinergic system influences the inflammatory response, controlling the release of TNF- α , IL1 β , and IL-6, and the non-neuronal acetylcholine synthesis and release machinery is unregulated in the inflammatory process [41]. Additionally, cardiovascular damage caused by excessive stimulation of the sympathetic nervous system and the renin-angiotensin system, as well as its receptors (α - and β -adrenergic receptors and AT1), appears to be mediated through activation of pro-inflammatory response. The migration of innate or adaptive immune cells to the central nervous system can induce excitation of hypothalamic and paraventricular nuclei and caudal and ventrolateral medullary

neurons that cause central sympathetic excitation [42, 43]. Interestingly, vagal activation may suppress inflammation [44], and physical exercise can contribute to greater vagal control [45], thus preventing important cardiovascular risk factors.

Considering that levels of cardiorespiratory fitness and muscle strength are inversely associated with the incidence of cardiovascular disease and all-cause mortality [27, 28], increasing levels of physical activity is crucial for the integrity of cardiovascular health, especially during the COVID-19 pandemic.

3. IMPACT OF STRESS ON CARDIOVASCULAR HEALTH

COVID-19 pandemic is associated with adverse consequences for mental health [46]. This situation significantly increased levels of panic, stress, and anxiety [47]. One study evaluated and compared several unhealthy behaviors during the lockdown period with the negative mood scale. The authors pointed out that poorer diet, poorer sleep quality, and physical inactivity were linked to a more-negative mood [10]. In Brazil, the cluster of unhealthy behaviors increased substantially and was associated with poorer mental health during quarantine [8]. In Spain, younger individuals with chronic diseases reported elevated symptoms of anxiety, stress and depression [48]. Social isolation, combined with fear of contagion and information overload, can also culminate in chronic stress related to a mental health burden. In addition, social isolation has been pointed out as a harmful factor to the autonomic regulation of the heart. This impairment is associated with high levels of cortisol and epinephrine, the main molecular markers of stress [15, 49]. It is already established that chronic stress is an important modulator of immunity; therefore, this factor can directly influence the probability of infection [50], as well as cardiovascular health. Stress in adulthood can trigger cardiovascular diseases in individuals who already have a high burden of atherosclerotic plaque. Besides, chronic stress can be a determining factor in the prognosis of pre-existing cardiovascular diseases [51]. High stress is also associated with an increase in the number of several infections, including influenza and other agents, and with cardiovascular damage. Evidence shows that chronic stress predicts coronary heart disease and socially isolated or lonely individuals have an increased risk of the first event of this type of disease [15]. Short-term emotional stress can also act as a precursor to cardiac injuries in individuals with advanced atherosclerosis [15].

Quarantine during the COVID-19 period resulted in some long-term effects on cardiovascular disease, mainly related to unhealthy lifestyle, anxiety and stress [52]. In fact, COVID-19 patients presented a high level of post-traumatic stress symptoms and studies with the general public revealed lower psychological well-being during the quarantine period [53]. The literature points out several mechanisms that associate stress with cardiovascular risk [15]. Stress culminates in increased cortisol and decreased heart rate, suggesting an important effect on the autonomic and neu-

roendocrine systems [15, 16]. The associated mechanisms include ANS hyperactivity and humoral changes, resulting in endothelial dysfunction, sympathetic activation and related increases in blood pressure and pro-inflammatory and procoagulant responses [15]. Especially the peripheral sympathetic nervous system plays an important role in the cardiovascular response to stress, innervating the heart, vasculature and adrenal medulla. This response occurs through the adrenal medulla, which systemically releases catecholamines (*e.g.*, epinephrine) and through the sympathetic nerve terminals, which innervate the vasculature and release norepinephrine. In this sense, the sympathetic nervous system is responsible for chronotropic and inotropic effects *via* β 1-adrenergic receptors and pressor effects *via* α 1-adrenergic receptors. In addition, the sympathetic nervous system also has immunological effects, including the release of interleukin-6 [54]. The inflammatory cascade related to oxidative imbalance may also explain the cardiovascular changes induced by stress [55]. In summary, the autonomic imbalance and the consequent increases in blood pressure and inflammation might favor the atherosclerotic process and cardiovascular diseases [15, 54]. Therefore, some clinical guidelines already point to stress as a target for cardiovascular disease prevention [51]. The relationship between physical inactivity, stress and cardiovascular diseases is illustrated in Fig. (1).

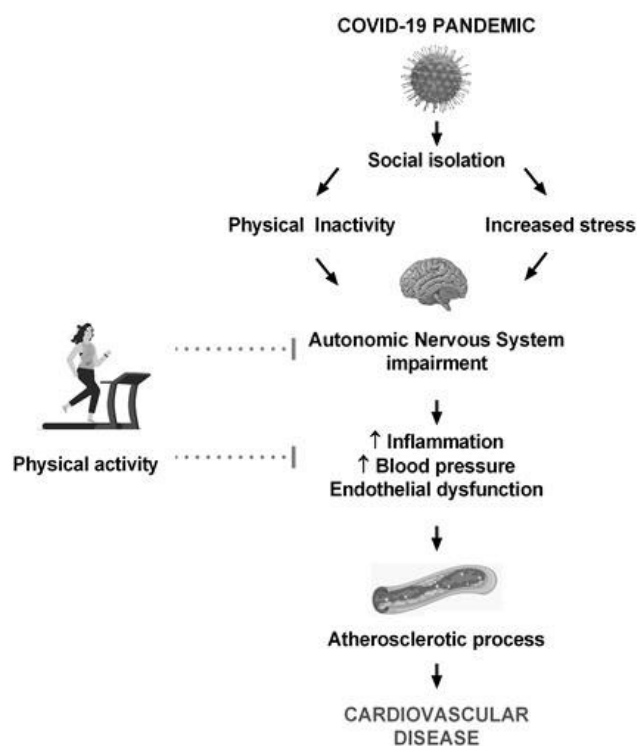


Fig. (1). Relationship between physical inactivity, stress and cardiovascular risk. Image created with Freepik.com.

On the other hand, studies show that increased physical activity culminates in reductions in distress [56]. Additional-

ly, both aerobic and resistance training results in reductions in psychological distress [57]. In this sense, it is clear that better control of stress and associated cardiovascular risks are crucial for preventing cardiovascular diseases.

4. IMPORTANCE OF PHYSICAL TRAINING ON CARDIOVASCULAR HEALTH AND STRESS MANAGEMENT

Several studies have shown the beneficial influence of physical exercise in the prevention and treatment of cardiovascular diseases [24, 58] such as improved exercise capacity, heart rate, endothelial function, autonomic nervous system function and blood pressure, reduced inflammatory cytokines, and reduced mortality [24, 45, 58]. Physical exercise is also associated with a 28% lower incidence of atrial fibrillation [59, 60]. Aerobic training is a common type of intervention that includes walking, running, cycling, and swimming. It has been showed that these training modalities increase peak work capacity and reduce all-cause mortality. For example, in patients with stable coronary artery disease, 3 × 1-hour aerobic training sessions at 75-80% of the peak heart rate for 6 weeks can increase the peak work capacity by 21% [61]. Aerobic training also reduces blood pressure, which is one of the main risk factors for cardiovascular events. It has been shown that aerobic training performed 90-150 min/week at 65% -75% heart rate reserve can decrease 5-8 mmHg of systolic blood pressure in hypertensive patients and 2-4 mmHg of systolic blood pressure in normotensive patients. On the other hand, resistance training performed 90-150 min/week at 50% -80% of 1 maximal repetition, 6 exercises, 3 sets/exercise, 10 repetitions/set can decrease 4mmHg of systolic blood pressure in hypertensive patients and 2mmHg of systolic pressure in normotensive patients [24].

Given the benefits above mentioned, guidelines for the prevention and rehabilitation of cardiovascular diseases from leading international societies suggest that healthy individuals and cardiovascular patients should undergo physical training [61]. According to the American College of Cardiology / American Heart Association, aerobic training is generally very safe, and sedentary individuals should start an exercise program at lower intensities and gradually progress to the recommended levels [61]. The European Society of Cardiology indicates moderate to vigorous intensities lasting 30 min/session for 3-5 days/week, reaching at least 150 min / week [62]. The Report of the American College of Cardiology / American Heart Association pointed out that in order to decrease cardiovascular risk, adults should perform at least 150 minutes per week of moderate-intensity aerobic training or 75 minutes per week of vigorous-intensity aerobic training [24]. Specifically, aerobic training for at least 3 days/week for 20-60 min/session with 10 to 15 min warm and cold, at intensities between 40 and 80% HR reserve is recommended [63]. On the other hand, resistance training improves muscle strength, which is also a significant predictor of risk factors and prognosis for cardiovascular diseases. Thus, including 15 to 20 minutes of resistance training twice a week for large muscle groups, in combination with aerobic

training is recommended [63]. Elderly adults who are unable to meet physical training recommendations are encouraged to be as physically active as their conditions allow [11].

Another potential ally for improving health in pandemic COVID-19 times as it culminates in benefits for cardiovascular and lung health is inspiratory muscle training. It was showed that 12 weeks of inspiratory muscle training at 30% of the maximal inspiratory pressure increased autonomic modulation, and expiratory, inspiratory, and exercise capacity in patients with the chronic obstructive pulmonary disease [64]. Besides, a systematic review pointed out that inspiratory muscle training performed at low intensities can chronically increase the parasympathetic modulation and reduce sympathetic cardiac modulation in patients with diabetes, hypertension, and chronic heart failure [65]. Also, inspiratory muscle training set at 50% of maximum inspiratory pressure, every day for 4 weeks, increased the heart rate variation and improved the 6-minute walk test and the resting heart rate in older women [66].

Physical training (aerobic and resistance training) is also related to the reduction of general psychological suffering. The study of LeBouthillier & Asmundson (2017) randomized 48 participants with anxiety-related into 3 groups: aerobic training group, resistance training group, and waitlist. Training sessions were performed three times a week for 4 weeks [57]. The aerobic training consisted of 40 minutes spin cycling with an intensity of 60-80% age-adjusted maximum heart rate reserve, while resistance training consisted of 2-3 sets of 10-12 repetitions to exhaustion. This study showed improved general psychological distress and anxiety with aerobic training, while resistance training improved anxiety sensitivity and distress tolerance [57]. Similarly, the critical influence of physical exercise on the perceived stress has been observed. A study with a heterogeneous group of 988 individuals looked at relationships between exercise frequency and the Perceived Stress Scale and showed that the reduced perceived stress was modest but significantly associated with aerobic exercise frequency [67].

It is noteworthy that other strategies can help controlling stress. Complementary and alternative medicine (CAM) practices can be an important strategy for stress control and cardiovascular health during the isolation period [68, 69]. Yoga increases vagal tone, reducing arrhythmia burden and improving hemodynamic parameters [68]. This practice is also associated with reduced evening and waking cortisol, systolic blood pressure, resting heart rate, and high-frequency heart rate variability [69]. In addition, Yoga, can increase the positive mental health of adults from non-clinical populations. Therefore, this practice contributes to a significant increase in psychological well-being when compared to no intervention [70]. Corroborating this data, a meta-analysis showed that Mind-Body exercises (*i.e.*, Tai Chi / Yoga) can be an alternative method to reduce stress in people who live under high stress or negative emotions and this reduction may be attributed to sympathetic-vagal balance [71]. Finally, mindfulness-based stress reduction is also able to decrease the perceived stress scale of healthy individuals [72].

Regarding the effects of exercise on cardiovascular parameters associated with stress, a study aimed to evaluate the effects of exercise training and weight loss on blood pressure associated with emotional stress during daily life. Interestingly, exercise, especially when combined with weight loss, reduces blood pressure levels at rest in situations that typically elevate blood pressure, such as intense emotional distress. These participants performed a supervised exercise program 3-4 times/week at 70-85% of their heart rate reserve. The protocol consisted of 10 minutes of warm-up exercises, 35 minutes of cycling and walking, and 10 minutes of relaxation exercises. In addition, this group participated in a behavioral weight management program, which consisted of approximately 26 weekly meetings, aiming at weight loss of 1 to 2 lb/week by reducing caloric and fat intake [73]. Additionally, 11 weeks of aerobic training performed 3 times/week, 30 minutes/day, reduces heart rate in situations of psychological stress [74].

Although these data indicate that particular importance must be given to physical exercise during the COVID- pandemic [1], the difficulty in keeping physically active in isolation and stress might result in cardiovascular damage and increased risk factors for other comorbidities [19, 50]. Therefore, what strategies could be taken to maintain the level of physical activity safely with social isolation measures?

In times of pandemics, when gyms are closed and contact with other people should be avoided in some countries, a home-based exercise strategy can be an exciting alternative to maintaining/improve cardiovascular health. It has been shown that home-based exercise training can improve several cardiovascular variables such as resting blood pressure, cardiac output, and heart rate in health normotensive males [75]. A long-term home-based exercise program improves the functional capacity, blood metabolic profile, and blood pressure of hypertensive patients [76]. Finally, inspiratory muscle training can reduce resting blood pressure and increase inspiratory muscle strength, lung capacity, and arm exercise duration in older people with well-controlled isolated systolic hypertension [77]. Nevertheless, we emphasize the need for further studies to evaluate home-based training proposals for specific populations (hypertensive patients, heart disease patients, diabetic patients, among others) who need to maintain social isolation to reduce the risk of COVID-19 morbidity.

5. HOME-BASED EXERCISE PROPOSAL FOR CAR-

DIOVASCULAR RISK PREVENTION DURING THE COVID-19 PANDEMIC

As previously mentioned, some detrimental effects of lockdown on health (*i.e.*, psychological distress and physical inactivity) during the COVID-19 pandemic period can induce maladaptation to the cardiovascular system [7, 10]. Thus, home-based physical activities that are feasible even in lockdown moments and that promise to help patients deal with the situation can be an important strategy for the pandemic period [7]. In this last session, we provide a suggestion of a feasible physical training recommendation for cardiovascular risk prevention during the lockdown period.

5.1. Aerobic Training

We propose aerobic training of moderate-intensity (12-16 on the Borg scale or 50-70% of heart rate reserve for sedentary individuals or 60-70% of heart rate reserve for trained individuals), which can include walking/running on the treadmill or in large places in the house and/or cycling on the exercise bike if the individual has this device. Jumping rope is also an interesting activity to do indoors. The suggested frequency is 3-5 times/week, totaling at least 150 minutes/week. It is also suggested that the individual start the training with 30 minutes/day, being able to progress up to 40-60 min a day, increasing 5 - 10 minutes every 1-2 weeks Table 1. In addition, stairs can be used to exercise the lower limbs and, depending on the speed, can be used for aerobic training [7].

5.2. Resistance Training

We suggest dynamic resistance training with body weight, free weight, elastic band or machine exercises if the individual has. The recommended frequency is 2-3 times/week, 2-3 sets, 8-10 exercises for large muscle groups (squat, push-up, sit and stand, split squat, straight abdominal, oblique abdominal, exercises with elastic band, among others) with an intensity of 12-16 on the Borg scale.

5.3. Inspiratory Muscle Training

We also suggest the inspiratory muscle training at 30% of maximal inspiratory pressure, 3 times a week, using a Threshold Inspiratory Muscle Training device. If the individual does not have this device at home, other alternatives devices (*i.e.*, EMST 150, Threshold Pep, Pflex Inspiratory Muscle Trainer) easily found in pharmacies or purchased online can be used.

Table 1. Home-based exercise protocol to improve cardiovascular health during COVID-19 pandemic.

Type	Aerobic Training	Resistance Training	Inspiratory Muscle Training
Exercises	Walking, running cycling, jumping rope	8-10 exercises for large muscle groups including: squat, push-up, sit and stand, split squat, straight abdominal, oblique abdominal, exercises with elastic band	Threshold Inspiratory Muscle Training (or others advices)
Frequency	3-5 times / week	2-3 times/week	3 times/week
Intensity	Moderate intensity	2-16 on the Borg scale	30% of maximal inspiratory pressure
Duration	At least 30 minutes/day	2-3 sets	-

5.4. How to Control the Training Intensity at Home

One way is to use the subjective effort scale (Borg scale), ranging from 0 to 20, where 0 represents rest and 20 represents exhaustion.

If the individual has a smartwatch or a frequency meter can use it to measure the heart rate. The 6-minute walk test and monitoring of resting heart rates are also interesting strategies. In addition, the fact that the individual can speak during the activity suggests that the intensity is moderate.

5.5. Care During Training

Individuals should avoid extremes of temperature and take days off. Importantly, individuals who show symptoms of COVID-19 must rest for ≥ 10 days from the onset of symptoms and another 7 days from the “cure” of the symptoms. Extra care should be taken by hypertensive patients: to avoid Valsalva maneuver, to avoid concentric fatigue, and to avoid apnea.

Individuals should also beware of excessive exercise. When the balance between high-load exercise sessions and the appropriate recovery period is interrupted, overtraining can lead to increased production and release of pro-inflammatory cytokines (*i.e.*, interleukin 6, tumor necrosis factor- α and interleukin 1 β) [78]. Overtraining can also result in pathologic cardiac hypertrophy [79] and arrhythmias (atrial fibrillation) [80].

During exercises on the stairs, individuals with compromised balance should hold on to the rails. For this practice, the use of gloves is recommended and hand washing is essential [7]. Lastly, we also emphasize the importance of continuing medical monitoring and follow-up by a physical education professional, even if remotely.

CONCLUSION

Sars-COV-2 pandemic is a health crisis culminated in high mortality and morbidity. In an attempt to reduce viral spread, governments adopted preventive measures that included social isolation. A home-based training protocol could be an interesting and effective strategy for the population who need to remain physically active and safe at home.

ABBREVIATION

COVID-19 = Coronavirus Disease 2019

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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