Review Article

The impact of sedentary lifestyles and physical activity on post-COVID syndrome: Adipose tissue and immune system interactions

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Abstract

Research indicates that a sedentary lifestyle significantly contributes to the development of post-COVID syndrome (PCS), characterized by persistent symptoms following acute COVID-19 infection. Engaging in regular physical activity is essential not only for mitigating these risks but also for enhancing recovery from COVID-19. Studies have shown that individuals who maintained high levels of PA before and after infection experienced fewer and less severe symptoms associated with PCS. Specifically, exercise training has been identified as a critical intervention for improving muscle function and modulating adipokine levels—signaling proteins released by adipose tissue that play a role in inflammation and metabolic regulation. Given the complex pathogenesis of PCS, which involves various physiological and psychological factors, it is imperative to incorporate structured exercise regimens into rehabilitation programs for affected individuals. Aerobic endurance training has demonstrated significant benefits in improving exercise capacity, reducing fatigue, and enhancing overall quality of life in PCS patients. Furthermore, high levels of PA are associated with improved immune function and lower rates of reinfection. In conclusion, promoting mandatory physical activity during and after pandemic conditions is vital for reducing the burden of post-COVID syndrome and enhancing public health outcomes. This review underscores the necessity for healthcare providers to advocate for exercise as a primary strategy in managing post-COVID symptoms and preventing future chronic diseases linked to sedentary behavior during different pandemics.

Key Words: **COVID-19; Sedentary lifestyle; Physical activity; Inflammation; Immune system, Adipokine**

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Introduction

On February 2, 2021, the coronavirus-19 (COVID-19) pandemic has affected more than 100 million people around the world, according to the World Health Organization (WHO) report (Organization, 2020). In Italy, as of August 31, 2020, more than 260,000 cumulative confirmed COVID-19 infections were reported with an overall fatality rate of 13.8%, making Italy the first European country to be affected by COVID-19 (Ferroni et al., 2020). On January 7, 2020, a new case of coronavirus was identified in China (Bernacer et al., 2021). Less than 30 days later, on January 30, 2020, the WHO declared a Public Health Emergency of International Concern. In less than two weeks, on February 11, 2020, the new virus was named SAR-CoV-2, as was the disease it causes COVID-19. Thirty days later, on March 11, 2020, the WHO declared a pandemic.

In Spain, on February 26, 2020, the first official case of locally transmitted COVID-19 infection was declared in Seville, Spain, believed to be from a German tourist in La Gomera, the Canary Islands, diagnosed on February 1. Quickly, in Spain, the number of confirmed cases climbed from 84 on March 1 to 6,391, and by March 14, 2020, with daily new diagnosed cases peaked to 9,630, the State of Emergency was declared. Spain quickly declared national compulsory confinement. By early July, more than 250,000 infections and 28,368 deaths had been officially confirmed. Since then, between March 14 and early May, strict restrictions on human movement were declared throughout Spain. Between March 16, 2020, and June 2, 2020, Spain was one of the most affected countries in the world. Subsequently, authorities in large metropolitan cities like New York City, San Francisco and Los Angeles, USA, London, England, Venice and Milan, Italy, Sydney, Australia, and Wuhan, China declared compulsory emergency lockdown (stay home), restricting all outdoor activities and travel. Although COVID-19 loads are uniformly distributed among individuals in all age groups (Garg et al., 2020; Klein et al., 2020), reports ind-

-icate that there is a higher prevalence among the elderly and among those with comorbidities, such as hypertension, diabetes, obesity, respiratory diseases, heart disease, and immunocompromised patients (Williamson et al., 2020).

On "beliefs" during different stages of emergency such as COVID-19 pandemic around the world, extraordinary circumstances such as exogenous shock like wars or natural disasters like the N1H1 and COVID-19 pandemic can change people's beliefs by which people can precede to the development of prosocial (i.e., strength ties to the community) or antisocial beliefs (i.e., create divisions and suspicious between people and groups), both of which influence attitudes and behaviors. The 2009 H1N1 (swine flu) pandemic confirms that shared threats can improve attitudes towards the government and medical organizations, leading toward increased adherence to health recommendations and guidelines (Bernacer et al., 2021).

Attitudes and beliefs can change over time. Under usual circumstances, adjustments follow persuasive messages, role-playing, or the acquisition of new information. However, traumatic events can also trigger change in one's global "beliefs" and "attitude". There are many cases of change in beliefs after a life-threatening outbreak of a disease like the "Spanish influenza" in Canada. A pandemic also has the potential to produce widespread changes in people's belief systems and can affect at the individual level or the aggregate level. The aggregate level implies that the entire population is affected through legislation to stay at home, lockdown of the economy, restrict movement and interactions in public places like public parks, gyms, and sports arenas, as well as personal freedom of choice to dine out with friends in restaurants, and about the public news information on the infections and the extraordinary death toll.

The COVID-19 pandemic has significantly impacted physical activity levels and increased sedentary behavior globally. This shift has profound implications for public health, particularly concerning obesity and related metabolic disorders linked to altered adipokine secretion. Addressing these issues through public health initiatives promoting physical activity is essential to mitigate the long-term health consequences of this pandemic-induced lifestyle change.

Also despite the belief that lockdown during the COVID-19 pandemic is healthy for the community, can we humans tolerate the inactivity or sedentary lifestyle imposed on us in a belief that lockdown restrictions are expected to ensure physical health (not getting sick), healthy community, and lower the burden of disease risk?

Purpose of the study

A pandemic lockdown means movement restrictions and increased physical inactivity leading to higher risk for chronic disease manifestations such as cardiovascular disease, dyslipidemia, lowering the immune response including cancer, high blood pressure, diabetes, obesity, depression, and insomnia. Most of the listed diseases are the consequence of physical inactivity or sedentary behavior. The purpose of this review is to present the health benefits of physical activity and clinical issues related to physical inactivity and sedentary lifestyle on chronic disease risk and severity of the disease manifestations, all of which are preventable with optimal physical activity. Also we investigate interactions between muscle and adipose tissue in the context of sedentary lifestyles during different pandemics.

Sedentary behavior and health

Sedentary behavior is one of the health consequences that causes long-term irreparable damage to the human body. The prevalence of sedentary behaviors has been increasing among the developed countries such as the USA, England, Canada, and Australia (Bakrania et al., 2018; Van Dyck et al., 2012; Warren et al., 2010). Physical inactivity causes damage to the body organs (De Geus et al., 2014). One of the main organs affected by physical inactivity or sedentary lifestyle is the skeletal muscle. Muscle atrophy (also known as sarcopenia in older persons or bed rest during prolonged illness) usually occurs one to two weeks after the onset of physical inactivity or bed rest (Deane et al., 2021). Aside from the negative effects of muscle atrophy, it has a negative impact on bone and balance (Bettis et al., 2018). Physiologically, during physical inactivity muscle tissue suffers from impaired glucose-fat metabolism, which can reduce insulin sensitivity and ultimately induce widespread related metabolic diseases. In addition, physical inactivity has been shown to reduce cardiac output and plasma volume, thereby reducing systemic blood flow and increasing the activity of the sympathetic nervous system, all of which negatively affect cardiovascular function, including blood pressure, resting heart rate and arrhythmia (Lippi et al., 2020; Nystoriak & Bhatnagar, 2018). Inactivity also provides the basis for inflammation by weakening the immune system, because in a sedentary lifestyle, adipose tissue increases and weakens the immune system, which may lead to various types of cancer (Passos et al., 2017; Pratapwar et al., 2020).

The spread of COVID-19 has significantly increased the sedentary lifestyle (Hall et al., 2021; C. Zheng et al., 2020), leading to multiple health consequences, including cardiovascular diseases, type 2 diabetes, and other types of degenerative diseases, particularly affecting the health of the elderly. Sedentary behaviors have a wide range of adverse health

effects; disorders such as osteoporosis, dementia, and depression are associated with a sedentary lifestyle (Knight, 2012; Tremblay et al., 2010). Therefore, avoiding sedentary behaviors and increasing physical activity are both critical for promoting personal health.

Prior to 2019, studies have shown the developed industrial societies as the major by-product of a sedentary lifestyle and the harmful effects on human health (Bauer & Vocke, 2016; Martin-Merino, 2021). However, with the identification of COVID-19 and the demand for health policies with multiple quarantines around the world, researchers have found that this and other pandemic diseases can lead to the increase of sedentary behavior in different communities. It should be noted that during quarantine, people are sitting much longer than before the COVID-19 pandemic (Sañudo et al., 2020). Prolonged physical inactivity causes more damage in old age, such as reducing quality of life, increasing inactivity treatment costs, and increasing future mortality (Cunningham et al., 2020). The WHO has recommended that 150 minutes of weekly moderate-intensity exercise training can be effective in preventing damage caused by a sedentary lifestyle (Bouchard et al., 2015). Therefore, it is necessary to understand the consequences of a sedentary lifestyle and the beneficial effects of exercise training to control sedentary lifestyle-related health consequences, especially during the COVID-19 pandemic.

Sedentary lifestyle, obesity, Adipokine and inflammatory factors

Obesity is often both a consequence and a contributor to sedentary lifestyles (Figure 1). It is defined by excessive fat accumulation that presents health risks. Obesity alters the secretion of adipokines—hormones produced by adipose tissue. Increased fat mass leads to elevated levels of pro-inflammatory adipokines like leptin and tumor necrosis factor-alpha (TNF-α), while reducing protective adipokines such as adiponectin (Allison et al., 2012; Inam et al., 2023). This imbalance exacerbates inflammation and metabolic dysfunction. The inflammatory response associated with obesity contributes to the development of insulin resistance and other metabolic disorders. Chronic inflammation is implicated in the progression of various diseases, including CVD and cancer (Park et al., 2020). Adipokines play a critical role in mediating the effects of obesity and sedentary behavior. It has been show that Leptin hormone regulates energy balance but can promote inflammation when secreted in excess due to obesity. Higher levels of leptin are associated with increased TNF-α production (Inam et al., 2023). Typically, anti-inflammatory, adiponectin levels decrease with increased fat mass. Low levels are linked to higher risks of metabolic syndrome and cardiovascular issues (Inam et al., 2023). The secretion patterns of these adipokines are influenced by physical activity levels. Sedentary individuals often exhibit unfavorable ratios of adiponectin to leptin, indicating heightened inflammatory states (Figure 1).

Mortality rates in covid 19 and other contemporary diseases

Most COVID-19 infected patients have mild symptoms (Wu & McGoogan, 2020), but 18% - 33% of hospitalized patients

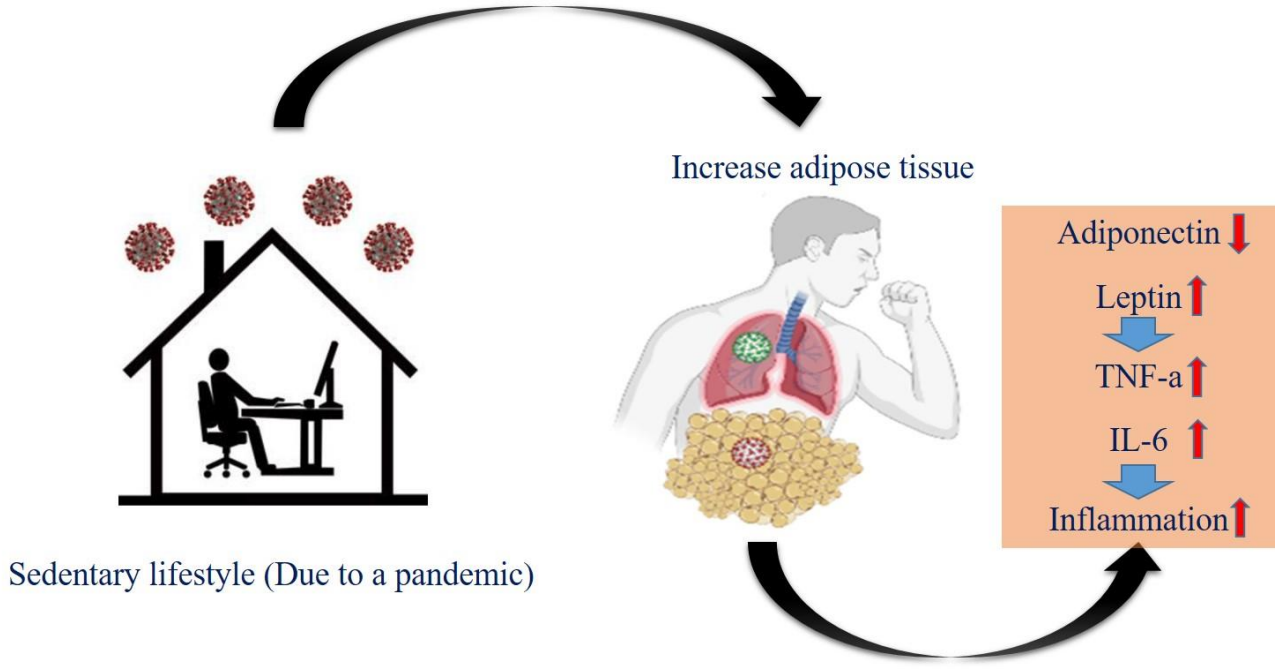
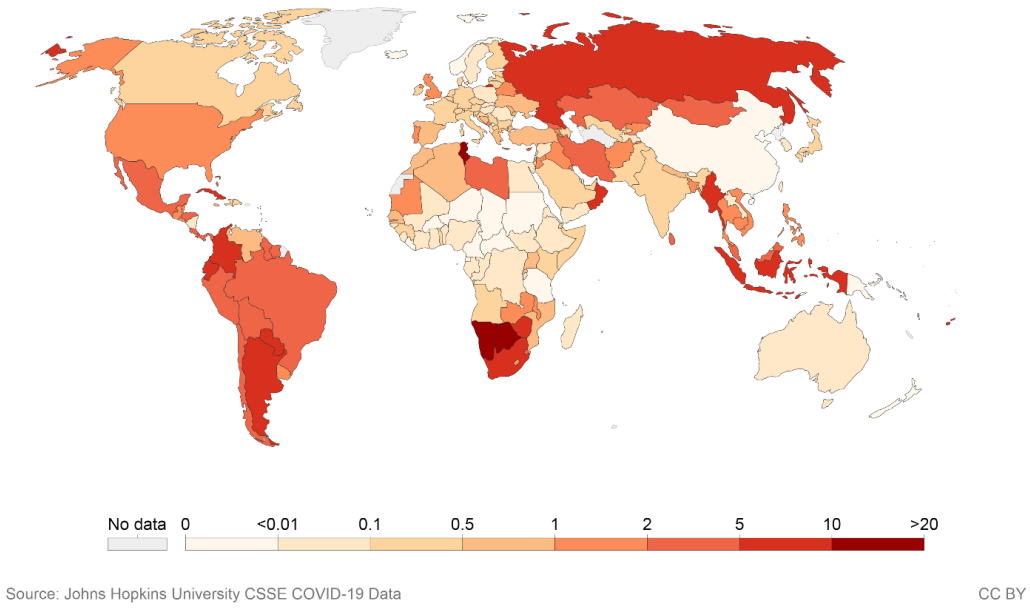


Figure 1. The effects of sedentary lifestyle on obesity and inflammatory factor.

required mechanical ventilation, and up to 20% of the hospitalized patients die (Gold et al., 2020; Goyal et al., 2020; Richardson et al., 2020). The reported mortality is often attributed to the virus load because hospitalized patients with severe COVID-19 infection have been shown to have higher viral loads than hospital-admitted patients with mild symptoms (Liu et al., 2020; S. Zheng et al., 2020).

Studies have shown that COVID-19 mortality rates increased exponentially with age (Promislow, 2020; Sargiacomo et al., 2020; Zhavoronkov, 2020). The exact reported mortality rate varies because of inaccurate or inconsistent vital statistics records use on testing and treatment interventions among the countries in the world. The fact is that COVID-19 mortality increases exponentially with age because the elderly has more

a)



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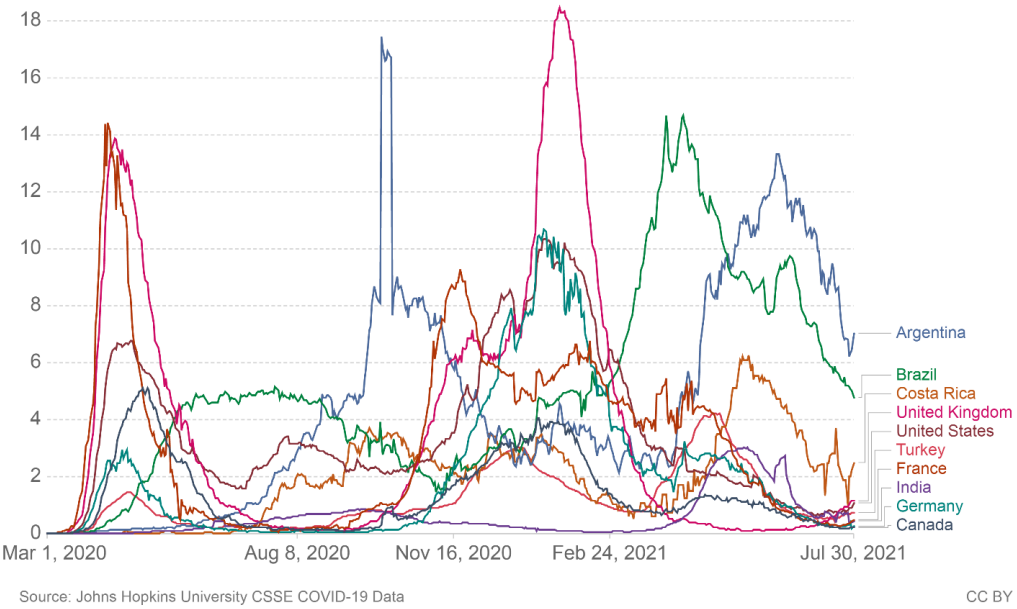

Figure 2. Shown is the rolling 7-day average (Figure 2a & Figure 2b). Limited testing and challenges in the reported mortality is often attributed to the virus load of the cause of death and the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19 (From Our World in Data).

multiple comorbidities. Also, the COVID-19 mortality rates in men are twice as high as that in women (Jin et al., 2020; Palaiodimos et al., 2020). Figure 2a (Johns Hopkins University CSSE COVID-19 data and Figure 2b (Our World in Data). In addition to age and gender, severe COVID-19 is associated with severe inflammation, cytokine storm, lung, heart, and kidney damage all of which are effectives in increasing mortality.

For example, in response to virus replication, monocytes and macrophages penetrate the lungs and cause inflammation and excessive secretion of cytokines and inflammatory factors (Yang et al., 2020; Yao et al., 2020). The factors leading to leukocyte uptakes, vascular permeability, and edema causing further lung damage (Rothan & Byrareddy, 2020; Vaninov, 2020). This high inflammation rate increases coagulation and thrombosis leading to further intravascular coagulation (Dolhnikoff et al., 2020). Coagulation causes damage to distant organs such as the kidneys and heart, both of which exacerbate the disease etiology (Siddiqi & Mehra, 2020). Most of all, high cell activity and excessive systemic inflammation lead to cell depletion, including lymphocytes which is associated with poor or weakened immune system, and further penetration of the virus, which increases the death rate.

COVID-19 and sedentary lifestyle

The Covid-19 pandemic required people to stay at home to quarantine for long periods of time as the best disease prevention public health strategy. Over time, this staying at home quarantine restricting outdoor movements has become a lifestyle behavior. Prolonged stay-at-home quarantine behavior has led to manifesting many sedentary behaviors such as long-term sleep, watching TV, computer games, and eating more food, all of which reduced mobility and promoted irreparable harm to the health of all age groups. The recommendations from the public health experts are to minimize or avoid sedentary activity during the stay-home quarantine, including active rest, getting up and walking at home, and doing online exercises. The fact is that the COVID-19 pandemic has had an overall negative effect on our physical and mental health, resulting in a 28.6% increase in sedentary behavior (Ammar et al., 2020). Numerous studies have reported an increase in the prevalence of inactivity during COVID-19. For example, children and adolescents in China regularly have been shown to participate in sports or recreation activities of 435 minutes per week, and since the spread of COVID-19, they spend 28 hours more on TV screen time per week (Xiang et al., 2020). Also, during the COVID-19 pandemic, children and young people in Canada have been shown to have lower levels of physical activity, higher sedentary behavior, and more sleep time (Moore et al., 2020). The negative impact of the COVID-19 pandemic in Canada resulted in 40.5% more sedentary behavior (Lesser & Nienhuis, 2020) and increased daily sitting time (Ammar et al., 2020). Adults in Australia also have been shown to exercise less and sleep more during the COVID-19 pandemic (Stanton et al., 2020).

Sedentary behavior is a global trend during the COVID-19 pandemic and is likely to continue even after we return to normal life post-COVID-19 (Hall et al., 2021). The effects of stay home quarantine inactivity are slowly increasing, and it is difficult to envisage what the physiological consequences will be in the future. For example, changes in the nervous-endocrine system and the immune system produce adaptive and compensatory reactions whose effects may persist for several generations, including inactivity and overeating and the development of chronic diseases (diabetes, obesity, and cardiovascular disease) in two or several generations (Nwanaji-Enwerem & Colicino, 2020). In other words, these lifestyle changes are currently occurring at this stage of the Covid-19 pandemic, and it is probable that there will be multiple physical and psychological consequences that will persist for a long time after the COVID-19 pandemic, including its impact on treatment costs and mortality worldwide.

The link with endocrine disorders was noticed quite early when it was found that patients with diabetes and uncontrolled hyperglycemia were at an increased risk of severe disease as well as mortality from COVID-19. However, the other endocrine manifestations of COVID-19 probably were subtler and information about them emerged more gradually over a period of time. Kumar et al. have reported endocrine abnormalities in COVID-19 patients with a focus on thyroid and adrenal function (Kumar et al., 2021). The recent literature provides evidence that male gonads may be potentially vulnerable to SARS-CoV-2 infection, recommending caution to pregnant women and couples planning natural pregnancy (Khalili et al., 2020).

Sedentary lifestyle and mortality rates

Sedentary lifestyle usually increases spontaneously during each period of time with the spread of a pandemic. For both healthy and sick people increasing sedentary lifestyle over a period of time can lower physiological age and increase mortality. During a pandemic quarantine period, sedentary behaviors due to staying home restriction and limited outdoor movements, activities such as time spent sleeping, watching TV, playing video games, or using a computer usually increase all of which does not require excessive energy expenditure usually is less than or equal to 1.5 MET (Howley, 2001).

According to the WHO, physical inactivity is a global health hazard. For example, physical inactivity ranks fourth in the list of risk factors for all-cause mortality after high blood pressure, smoking, and diabetes (World Health Organization - Health Report). Also, physical inactivity is the reason for 21-25% of breast and colon cancers, 27% of diabetes and 30% of atherosclerotic diseases (Booth et al., 2017).

Physical inactivity increases mortality, also influencing other risk factors, such as hyperlipidemia, diabetes, hypertension, and heart diseases. For example, studies have shown that the effect of physical inactivity on mortality is much greater than obesity (Ekelund et al., 2015) because inactivity itself is one of the reasons for the spread of obesity and increased blood lipids. Thus, physical inactivity and staying home quarantine can lead to disruption of diet and increase prevalence of overeating and calorie intake compared to an active lifestyle. Over the course of one's life (without quarantine), a person has more mobility and greater opportunity to engage in physical activity, such as walking, which increases the amount of energy expenditure. However, during stay home quarantine due COVID-19 pandemic, both inactivity and the prevalence of overeating lead to an increase in caloric intake and an increase in fat storage leading to increased blood fat levels. This can manifest hyperlipidemia which is considered one of the diseases with the highest mortality rate in the world.

Physical inactivity has been reported to stimulate visceral fat accumulation, inflammation, and metabolic disorders (Pedersen, 2017). High levels of triglycerides can exacerbate the harmful effects of fat. For example, the clinical manifestations of hyperlipidemia are mainly xanthoma due to lipid deposition in the dermis and atherosclerosis due to lipid deposition in the vascular endothelium (Feingold et al., 1989). Hyperlipidemia is the most dangerous risk factor associated with atherosclerosis (Ross & Harker, 1976). In addition, hyperlipidemia is a risk factor for stroke, coronary heart disease, myocardial infarction, and sudden cardiac death (Fan et al., 2018).

Cardiovascular risk factors such as high blood pressure, high total- and LDL- cholesterol, diabetes, excessive body mass index, low HDL-cholesterol, and obesity are usually present together in sedentary people (Carnethon et al., 2005). Recent studies on the prevalence of inactivity and cardiovascular disease have shown that inactivity is a potential risk factor for increased susceptibility to cardiovascular disease (Erlichman et al., 2002). In other words, sedentary behaviors increase the risk of cardiovascular mortality (Warren et al., 2010). It is reported that coronary artery disease (CAD) is the cause of death for one in every five people, and its annual cost is more than US$ 160 billion (Members et al., 2011). CAD is likely to cause death, especially in those over 35 years (Lerner & Kannel, 1986). Cardiovascular diseases are caused by inactivity or by having high levels of visc-eral adipose tissue and an increased risk of atherosclerosis or hypertension. Studies have shown that peripheral atherosclerosis alone or in combination with other atherosclerotic manifestations is a predictor of cardiovascular mortality (Ögren et al., 1993).

High blood pressure is a fatal and preventable risk factor for cardiovascular disease and is responsible for most cardiovascular deaths. High blood pressure is closely linked to a sedentary lifestyle. Note that there is a positive correlation between the prevalence of hypertension and stroke mortality (Wolf-Maier et al., 2003). Increased blood pressure due to sedentary lifestyle, especially in the elderly, leads to an increased prevalence of hypertension (Franklin et al., 1997). Aging with a combination of sedentary lifestyle can lead to overweight and obesity, increasing the prevalence of hypertension (Kearney et al., 2005). Therefore, physical inactivity, whether due to aging or poor lifestyle or quarantine due to the COVID-19 pandemic, is a risk factor for many diseases such as hypertension, diabetes, and cardiovascular disease (Chodzko-Zajko et al., 2009).

Other side effects of quarantine and inactivity include the induction of metabolic diseases, including diabetes and fatty liver. People with diabetes during quarantine can acquire the greatest damage due to lack of muscular activity, which plays an important role in controlling blood glucose. Diabetes and its complications affect quality of life and increase the economic burden of patients and society (Happich et al., 2008). For example, the prevalence of insulin resistance in developed countries is 15-20%. It is estimated that about 8% of the world's population is affected by diabetes mellitus (Bird & Hawley, 2017). Genetic predisposition, physical inactivity, and poor diet play a role in insulin resistance (Röhling et al., 2016). Insulin sensitivity decreases with inactivity (Booth et al., 2017; Pérez-Martin et al., 2001). Hemoglobin A1c (HbA1c) levels appear to be a major predictor of diabetes mortality. Thus, a 1% reduction in serum HbA1c leads to a 14% reduction in myocardial infarction and a more than 20% reduction in the risk of death from diabetes (Liu et al., 2019). Diabetes mellitus is now the ninth leading cause of death in the world. The increasing prevalence of type 2 diabetes has become common in most developed countries. A sedentary lifestyle is known as one of the most important causes of the prevalence of type 2 diabetes. Therefore, physical inactivity caused by the Covid-19 pandemic can incur irreparable costs by inducing metabolic disease.

Cachexia (muscle atrophy) occurs at different ages and is also a complication of quarantine and a sedentary lifestyle. Muscle disuse causes the onset of signaling pathways, including myostatin/Smad, IGF1-Akt-mTOR, E3 ligases of the ubiquitin-proteasome, Atrogin-1/MAFbx, and MuRF1, which mediate the adaptation of skeletal muscle protein to immobility and inflammation (Brooks & Myburgh, 2014). Therefore, regular exercise in the gym or at home can be used as a strategy to stre-

-ngthen muscle activity, control body weight, and other related health consequences caused by inactivity during (stay at home) quarantine due to COVID-19.

In summary, physical inactivity and sedentary lifestyles pose significant risks for health by contributing to chronic diseases and altering the secretion of adipokines. These changes can lead to metabolic dysfunctions that have lasting impacts on both physical and mental health. Addressing these issues through increased physical activity is essential for improving overall health outcomes.

Regular exercise training and health benefits

Due to the increase in time available during a pandemic such as Covid-19, regular exercise can be incorporated into your daily routine to avoid the side effects of the pandemic associated with physical inactivity. In recent years, the American College of Sports Medicine has initiated the concept that "exercise is a medicine," a phrase that is gradually gaining popularity. Evidence has shown that exercise can effectively prevent and treat chronic diseases such as heart failure, cognitive impairment, obesity, fatty liver, and other diseases. A study has shown that lifestyle intervention with physical activity was more effective than metformin (a blood sugar controlling drug) in reducing the incidence of type-2 diabetes (Group, 2002). Increased physical activity and exercise is the real “polypill” and there is research to support the claim for the prevention and management of many diseases (Bull et al., 2020). For example, adaptation to a healthy lifestyle, including adequate daily physical activity or exercise, has been shown to reduce cardiovascular mortality by 80% and cancer mortality by 40% (Xiao, 2020). There is more evidence to show that this relationship is dose-dependent, and even half of the recommended normal physical activity significantly reduces the risk factor of disease. A combination of increased physical activity or exercise and reduced sedentary behavior is likely to result in greater disease risk reduction (Owen et al., 2020).

Regular exercise training can prevent many chronic diseases (such as certain types of cancer, osteoporosis, type-2 diabetes, or high blood pressure). Also, studies have shown that regular exercise training is associated with an overall reduction in relative risk of premature death from any cause (Warburton et al., 2006). For example, active men were found to have their relative risk of death lowered by 50% compared to sedentary individuals (Myers et al., 2004), and middle-aged women were twice as likely to die if they were sedentary compared to those who exercised regularly. Therefore, exercise during a pandemic such as COVID-19 should be performed regularly. The reasons for this are because physical activity: 1) improves the ability to perform exercise (Lavie & Milani, 2011) without undue fatigue (Lavie & Milani, 2000), peak oxygen consumption (Saberi et al., 2017), and the anaerobic threshold (Pymer et al., 2020), 2) decreases total cholesterol, triglycerides and LDL-Cholesterol (Muñoz-Vera et al., 2017), insulin resistance (Kumar et al., 2019), body mass index (Pandey et al., 2017), metabolic syndrome (Myers et al., 2019), and high-sensitivity CRP (Fernandes et al., 2018), and 3) reduces anxiety (Voinea, 2017), hostility (Maier & James, 2014) and mental depression (Dale et al., 2019). Among the benefits to the cardiovascular system and disease-related financial burden of regular exercise training are lowering resting heart rate, improving blood rheology, and reducing hospitalization costs and mortality (de Souto Barreto et al., 2019). Therefore, regular exercise training during Covid-19 minimizes the physical and mental damage caused by a sedentary lifestyle.

Currently, researchers are attempting to determine whether there is a link between skeletal muscle contraction and improved health. For example, how skeletal muscle and exercise-induced adaptation occur in the heart, lung, liver, bone, and adipose tissue. Research has shown that exercise is beneficial for cardiovascular health. In addition, exercise is considered an effective therapeutic approach to preventing cardiovascular disease and diabetes (Kemps et al., 2019). Various studies have shown that optimal exercise prescriptions prevent cardiovascular disease and help maintain good health (Hannan et al., 2021; Lee et al., 2020). A physically active lifestyle in adulthood not only prevents cardiovascular disease independent of other risk factors but also may increase life expectancy in both sexes. This effect can be achieved with moderate-intensity levels of physical activity, and life expectancy without cardiovascular disease is greatly improved with high-intensity activity (Franco et al., 2005). Franco et al. also found that life expectancy for sedentary people in their 50s was 1.5 years shorter than those with moderate daily physical activity and more than 3.5 years shorter than those with high levels of physical activity (Franco et al., 2005). These differences were similar in terms of the severity of coronary artery disease (CAD) in both sexes and the number of CAD involvement, myocardial ischemia, angina severity, left ventricular function, and general health status (Braunwald et al., 2000). Accordingly, exercise training has been utilized as one of the main modalities of cardiac rehabilitation for the reduction in cardiovascular mortality and lowering of disease-related readmission to hospital, as well as reduction in psychological stress and CAD risk factors.

In addition, exercise and physical activity are effective as strategies used to lose weight, improve insulin sensitivity, appetite, serum omentin-1 concentration due to overweight and obesity. In addition, exercise-induced weight loss reduces serum concentration of vaspin, which may lead to inhibition of inflammatory processes and insulin resistance (Escoté et al., 2017). Exercise alone has been shown to be effective in preventing patients with type-2 diabetes, including improvements in the management of blood glucose levels, body weight, fat, blo-

-od pressure, cardiovascular disease mortality, and overall quality of life (Stanford & Goodyear, 2014). It has been shown that regular aerobic exercise improves structural, functional, and biochemical parameters in the cardiovascular system in individuals with and without hypertension (Cornelissen & Fagard, 2005). Physical activity is as important as medication in reducing cardiovascular mortality in patients with hypertension. For example, research has shown that regular exercise once a week is more effective than drug therapy in reducing hypertension-induced mortality in hypertensive patients (Brown et al., 2013). In general, a reduction of 5 mm Hg in systolic blood pressure (BP) with regular exercise has been reported. It was estimated that a 5 mm Hg decrease in systolic BP, can lower mortality from coronary heart disease by 9%, mortality from stroke by 14%, and decrease mortality from all causes by 7%. Therefore, regular exercise should be recommended for everyone, including people with normal blood pressure, prehypertension, and hypertension, especially during the COVID-19 pandemic.

For other metabolic diseases, including fatty liver, regular exercise, especially high-intensity interval training (HIIT), is highly recommended because regular exercise can control blood lipid levels, reduce liver damage, improve quality of life, and lower mortality. Therefore, regular exercise or HIIT during the COVID-19 pandemic is highly recommended. Table 1 shows studies with regular exercise training or physical activity on preventing chronic disease and lowering mortality in humans.

Exercise recommendations for active lifestyle during pandemic infections

Regular exercise training and an active lifestyle with different mechanisms can reduce disease risk factors and ultimately lower mortality risk (Figure 3).

Recommended exercise guidelines

Given the adverse effects of inactivity and sedentary lifestyle on health, the cost of treatment in each country, and the increase in future mortality, it is recommended that one should avoid a sedentary lifestyle during a pandemic infection. Therefore, during a pandemic, engage in a regular exercise program and follow the recommended guidelines below.

• Use a variety of exercise training modalities such as endurance, sprint, strength training, or in combination of both types of exercise. Regardless of whether participation in endurance, sprint, or strength training regimen, the adaptive response for induced increases in skeletal muscle GLUT4 expression in patients with type 2 diabetes are similar (Hargreaves, 2021).

• Do 150 minutes continuous moderate-intensity exercise, 30 minutes a day, 5 days per week.

• Activities such as walking, running, and cycling performed alone

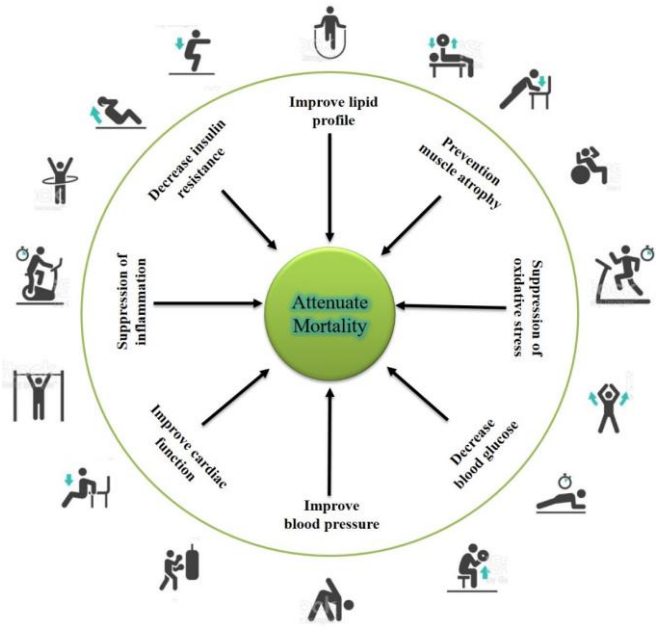

Figure 3. An active lifestyle and regular exercise training during the pandemic disease can reduce future mortality.

or in pairs (for mental health and to decrease anxiety) in a secluded or separated environment are recommended. However, during a pandemic such as COVID-19, competitive and vigorous exercise is not recommended.

• Do squats (because they involve large muscle groups) in accordance with the overload principle of training every day (3 sets of 30 repetitions).

• Do daily exercises such as rope-jumping that have a higher calorie intake.

• Even if you do not lose weight, do your exercise regularly because exercise training improves cardiovascular health and whole-body metabolism and helps maintain and improve mental health during the pandemic.

• People with various diseases during the pandemic are advised to develop individually formulated exercise program(s) under the supervision of an exercise physiologist or personal trainer (i.e., exercise type with optimal intensity, duration, and frequency based on the individual's physical condition to minimize or avoid contraindications and adverse effects).

Conclusion

A sedentary lifestyle has an adverse effect on health and can cause various diseases, reduced quality of life, and increase mortality. Therefore, during a pandemic such as COVID-19, engaging in exercise training on a mandatory basis as opposed to voluntary is highly recommended because so far, no therapeutic treatment alternatives other than exercise training that can effectively lower mortality from various diseases.

Table 1. The effect of an active lifestyle and regular exercise training on reducing health risk factors related to mortality.

References	Subjects and type of exercise	Positive results of exercise training	Conclusion
(Seip et al., 1993)	9-12 months of aerobic exercise training	↓ 13.2% CETP in women ↓ 14.2% CETP in men ↑ HDL	Decrease risk of mortality
(Kraus et al., 2002)	Control: 6 months High-intensity training: 8 months Low-intensity training: 8 months	Low intensity is better on lipid profile than high intensity: ↑ HDL ↓ VLDL ↓ LDL	
(Gadais et al., 2018)	Meta-analysis: consideration effects of aerobic exercise training	↑ HDL-C	
(Hazar et al., 2010)	24 middle-aged women (overweight) Performed aerobic exercise for 40 days.	↓ Cholesterol ↓ Triglyceride ↓ Bodyweight	
(Laaksonen et al., 2005)	4 years of exercise training	65-63% lower chance of developing diabetes	
(Duclos et al., 2015)	Considering 1766 diabetic patients with blood pressure	Blood pressure in active diabetic patients is significantly lower than in inactive diabetic patients	
(de Morais et al., 2015)	A clinical trial study on patients with diabetic hypertension	A course of maximal intensity aerobic exercise leads to an 8-hour reduction in blood pressure after exercise	
(Gondim et al., 2015)	6 and 12 weeks of moderate-intensity exercise training in overweight and fat subjects	↔HDL-C ↓ Leptin ↓ Insulin resistance ↑ Adiponectin ↓ Diastolic blood pressure ↓ Homocysteine ↓ IL-6	
(Cassidy et al., 2016)	HIIT for diabetic patients with DCM	↑ Systolic function ↑ Diastolic function ↓ Peak torsion Heart physiological hypertrophy	
(Boor et al., 2009)	10 weeks of treadmill running on obese diabetic rats	↓ Renal interstitial fibrosis ↓ Nε-carboxymethyllysine	
(Castro et al., 2019)	The effect of 12 weeks of resistance, aerobics and combined exercise training on diabetic rats	↓ Abdominal fat ↓ Blood glucose ↓ CRP ↓ IL-6 ↑ Serum adiponectin and omentin	
(Bohn et al., 2015)	Evaluation of the effect of exercise training on 18,028 T1DM patients	↓ HbA1c ↓ Diabetic ketoacidosis ↓ Dyslipidemia ↓ Hypertension ↓ Retinopathy ↓ Microalbuminuria	
(Balducci et al., 2006)	78 patients with diabetes without peripheral neuropathy Exercise group performs 4 hours of high-intensity exercise training per week (4 years)	↑ NCV ↓ Diabetes neuropathy	
(Marson et al., 2016)	A meta-analysis of 17 studies Consider the effects of 6 weeks (at last) of combined exercise training in overweight or obese children or adults	↓ Fasting insulin levels ↓ Insulin resistance	
(Kelley & Kelley, 2000)	A meta-analysis of 72 studies, with 4,000 non-athlete subjects doing aerobic exercise	↓ 3 mm Hg of rest BP ↓ 2.4 mm Hg of MBP	
(Whelton et al., 2002)	A meta-analysis with 54 studies involving 2,400 subjects. Considering the effects of aerobic exercise training.	↓ 3.84 mm Hg of SBP ↓ 2.58 mm Hg of DBP	

↓: Decrease, ↑: Increase, ↔: No change. Abbreviation. HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoproteins, IL-6: Interleukin-6, CRP: C-reactive protein, Hba1c: HbA1c, T1DM: Type I Diabetes Mellitus, HIIT: High-intensity interval training, NCV: Nerve conduction velocity, BP: Blood pressure. MBP: Mean blood pressure. Mm Hg: Millimeters of mercury, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

What is already known on this subject?

a sedentary lifestyle significantly contributes to the development of post-COVID syndrome (PCS), characterized by persistent symptoms following acute COVID-19 infection.

What this study adds?

During a pandemic such as COVID-19, engaging in exercise training on a mandatory basis as opposed to voluntary is highly recommended because so far, no therapeutic treatment alternatives other than exercise training that can effectively lower mortality from various diseases.

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