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THE IMPACT OF PHYSICAL ACTIVITY ON THE RISK AND SEVERITY OF COVID-19 INFECTION

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ABSTRACT:

Introduction: A rapid outbreak of SARS-CoV-2 in the past few years caused a significant increase in the number of upper respiratory tract infections throughout the world. Numerous public health institutions tried to control the COVID-19 pandemic, including mandatory mask wearing, vaccinations, increased frequency of using disinfectants or compulsory lockdowns. Lockdown interventions were necessary, although they lead to insufficient, comparing to the international recommendations, levels of physical activity, which could trigger an elevated susceptibility to diseases of affluence.
Purpose: Regular aerobic exercise may suppress inflammation, boost innate immunity and result in enhanced protection against viral infections. This review aims to show the relationship between level of physical activity and the risk and severity of COVID-19 infection.
Material and methods: In December 2023, the Medline (PubMed) and Google Scholar databases were searched using following keywords: *physical activity, exercise, COVID-19, SARS-CoV-2, infection, mortality*. Records published in 2020 – 2023 in English were selected.
Brief description of the state of knowledge: SARS-CoV-2 virus infection occurs through respiratory droplet. The most common symptoms of the disease include fever, dry cough,

shortness of breath, fatigue and muscle pain. Laboratory tests show elevated inflammation factors and abnormal coagulation factors among people with SARS-CoV-2 infection. Limited physical activity promotes the development of various diseases, such as diabetes and obesity, which were the main causes of death during the SARS-CoV-2 pandemic. Regular physical exercises activate cells of the immune system, i.e. leukocytes, lymphocytes and NK cells, such process is associated with a better cellular response to infection. Patients who regularly undertook physical activity of at least moderate intensity had better respiratory capacity and reserve, higher haemoglobin oxygen saturation levels, and were therefore less susceptible to hypoxemia. People who were more athletic before SARS-CoV-2 infection were less often hospitalized, admitted to the intensive care unit and had a lower risk of death compared to people leading a sedentary lifestyle. Due to its anti-inflammatory and anti-metabolic effects, obese patients also benefit from it. The least susceptible to SARS-CoV-2 infection were people who performed vigorous, high-intensity exercise.

Conclusions: Physical activity has a protective effect against severe SARS-CoV-2 infection. It is worth to consider, whether limiting physical activity and a sedentary lifestyle effectively fight viral infection. A recommendation to perform regular physical activity might be a simple way of protection against the high risk of mortality during the coming waves of the pandemic.

Keywords: *"physical activity" ; "exercise" ; "COVID-19" ; "SARS-CoV-2" ; "infection" ; "mortality".*

INTRODUCTION:

In the second half of December 2019 the information about outbreak of series of unknown-cause poneumonia cases in Wuhan city, Hubei Province, central China, has been spread all around the world[1]. SARS-CoV-2 *(Severe Acute Respiratory Syndrome CoronaVirus 2)*, a new type of virus, identified at Chinese Academy of Engineering, has been spreading at a hectic

pace[2]. At the beginning of March 2020 World Health Organization (WHO) announced that the massive infections of upper respiratory tracts have reached the pandemic level [3]. According to WHO date the number of infections reached 2 760 320 on June 28, 2021, including 53,666 deaths[4]. To reduce the rapid spread of the SARS-CoV-2, the goverment recommended mandatory mask wearing, vaccinations and compulsory lockdowns [41]. The lockdown intervention contributed to reduced levels of physical activity and unhealthy lifestyles [5,6]. A 30% reduction in physical activity was observed during COVID-19 quarantine, regarding sex and age [7]. It has been known for a long time that physical activity reduces the risk of diseases, including the risk of upper respiratory tract diseases [8,9]. Physical exercise may positively affect various cardiovascular risk factors including body weight, blood pressure, insulin sensitivity, lipid and glucose metabolism, heart function, endothelial function, and body fat composition [10]. Limited physical activity and an unhealthy lifestyle are associated with obesity, diabetes, hypertension and cardiovascular diseases (CVD), and these metabolic diseases are risk factors for severity and mortality in the course of COVID-19 [11,12].

AIM OF THE STUDY:

Large observational studies suggest that exercise itself may reduce mortality in a particular disease. Therefore, the question arises whether physical activity has a protective effect against SARS-CoV-2 infection and its severe course. Given the increased risk of COVID-19, the more severe course of the disease and the higher mortality rate, the following review aims to explore the impact of physical activity on the risk and severity of COVID-19 infection.

MATERIAL AND METHODS:

In December 2023, the Medline (PubMed) and Google Scholar databases were searched using following keywords: *physical activity, exercise, COVID-19, SARS-CoV-2, infection, mortality*. Records published in 2020 – 2023 in English were selected.

BRIEF DESCRIPTION OF THE STATE OF KNOWLEDGE:

Pathophysiology

Human CoronaVirus (HCoV) infects the upper and lower respiratory tract, especially in children, the elderly and patients with cardiac and respiratory disease[13]. Transmission of Sars-

Cov-2 virus is through the droplet route and, to a lesser extent, through contaminated surfaces. On average, 50% of infections can occur through pre-symptomatic carriers [14]. Typical symptoms of hospitalized patients include fever 38.5 - 39.0 ºC (70%-90%), dry cough (60%-86%), shortness of breath (53%-80%), fatigue (38%), muscle aches (15-44%), nausea/vomiting or diarrhea (15%-39%), headache, weakness (25%) and nasal leakage (7%). Lack of smell or lack of taste may be the only symptom in about 3% of Covid-19 patients [15]. X-rays or CT scans show unilateral or bilateral pneumonia. In laboratory tests, we will encounter abnormalities such as elevated inflammatory markers (erythrocyte sedimentation rate, C-reactive protein, ferritin, TNF - alpha, IFN-γ-IP-10, IFN-γ, IL-1B, IL-6, IL-8, IL-12 and MCP-1) and abnormal coagulation parameters, i.e. prolonged prothrombin time, thrombocytopaenia, elevated levels of the D-dimer [46% of patients], low fibrinogen levels [16]. The average recovery period in people without immune disorders is 2 to 3 weeks, and the median length of hospital stay in recovering patients is 10 days [16]. The diseases that most commonly contributed to death in COVID-19 patients were cardiovascular disease, diabetes, hypertension and obesity[17]. Limited physical activity during the pandemic enhanced their development[18,19,20,21].

Physical activity and the immune system in patients with COVID-19

In a randomised controlled trial from October 2021. the effects of moderate-intensity aerobic exercise were investigated on immune biomarkers, symptom severity and disease progression in patients with COVID-19 [22]. This study included 30 COVID-19 patients aged between 24-45 years old. Patients, diagnosed with SARS-CoV-2 infections were recruited from April 2020 to June 2020, based on a Turkish hospital in Istanbul. Inclusion criteria were a recent history of mild or moderate type of COVID-19. Mild COVID-19 included symptoms such as fever, cough, muscle aches, runny nose, fatigue, sore throat, sneezing or gastrointestinal symptoms: nausea, vomiting, abdominal pain, diarrhoea. Symptoms of the moderate COVID-19 included: pneumonia (cough, fever), without hypoxaemia, with changes present on chest CT. Exclusion criteria were fever below 38.3ºC and associated chronic diseases. Women using contraceptives were also excluded, as they impair immune function caused by contraceptives[23]. The researchers divided the participants into 2 groups . The research group, was to perform aerobic exercise for 2 weeks for 40 min per session, with a consideration of 3 sessions per week. Each session consisted of a 5-minute warm-up, 30 min of aerobic exercise at an intensity of 60-75% of the age-predicted MHR (Maximum Heart Rate) (MHR =

210 - age [bpm]) and 5 min of calming exercise. Patients in the control group did not exercise. This study aimed to test the effects of moderate-intensity aerobic exercise on immune biomarkers (leukocytes, lymphocytes, IL-6, IL-10, IgA, TNF-alpha), COVID-19 symptom severity and disease progression. The Wisconsin Upper Respiratory Symptom Survey (WURSS-24), also known as the Wisconsin Scale (patient-oriented illness-specific quality-of-life), was used to screen for symptoms.Participants completed the WURSS-24 before the start of the study and after 2 weeks. It is a validated and reliable method for assessing changes in quality of life during flu-like illness symptoms such as headache, body aches and fever[24,25]. At baseline measurements, there were no significant differences in the parameters studied. The number of leukocytes, lymphocytes and IgA after 2 weeks increased significantly in the study group compared to the control group. The large increase in lymphocyte counts in the study group may be due to the fact that aerobic exercise increases the recruitment of NK cells, T and B lymphocytes in the bloodstream. NK cells play a major role in fighting upper respiratory tract infections, leading to a reduction in the severity and progression of symptoms. Another point is that aerobic exercise activates the proliferation and readiness of macrophages, which inhibit viral proliferation in the airways [26,27,28]. An increase in macrophage numbers entails the production of chemokines and antiviral factors such as TNF-alpha and IFN-alpha, IFN -beta, which help recruit and activate other cell types to fight infection [27,29]. There was an increase in salivary IgA titres in the study group, which is known to be inversely related to the risk and severity of upper respiratory tract infection symptoms [30,31]. In addition, the Wisconsin Upper Respiratory Symptom Survey (WURSS) total score was significantly lower in the exercisers compared to the non-exercise group, demonstrating that physical activity protected against COVID-19 severity and reduced the risk of symptom severity, improving patients' quality of life. This study showed that two weeks of moderate-intensity aerobic exercise reduced the severity and progression of COVID-19-related disorders and improved quality of life.

Physical activity and respiratory capacity in patients with COVID-19

The protective effect of physical activity on COVID-19 severity is also presented in a retrospective cohort study from June 2021. [32]. Patients hospitalised during the first wave of the pandemic in a Spanish hospital were included in the study. Inclusion criteria were age between 18 and 70 years, fever above 38ºC, lung infiltrates visible on chest X-ray and the need for supplementary oxygen to achieve a saturation above 92%. Patients included in the study also had to fulfil laboratory criteria, including white blood cell count, CRP, ferritin and D-

dimers. Patients who were symptomatic but PCR-negative for SARS-CoV-2 infection were excluded from the study. Patients over 70 years of age were excluded from the study due to potential limitations in terms of physical activity. Baseline physical activity level, BPAL (Baseline Physical Activity Level) was assessed using the Rapid Assessment of Physical Activity Scale (RAPA) questionnaire, which has already been used in other publications[33,34]. RAPA is a nine-item questionnaire originally developed to assess the amount and intensity of physical activity in adults aged 50 years and older [34]. After discharge, all patients included in the study were contacted by telephone to complete the test. This test is divided into two categories:RAPA 1 - which assesses the intensity of aerobic exercise (score from 1 to 7) and RAPA 2, the type of exercise (muscle strength, flexibility or both.) For the needs of this study, only RAPA 1 was used and patients were divided into 2 groups - the first with a RAPA score of 1-3, i.e. sedentary lifestyle or light physical activity, and the second with a RAPA score of 4-7 - adequate, regular physical activity. Ultimately, 297 patients were included in group 1 and 223 patients in group 2. Group 1 had a significantly higher median age than group 2. Group 1 also had a higher prevalence of hypertension, renal impairment, chronic obstructive pulmonary disease (COPD), cerebrovascular pathology, liver disease and addiction. However, no differences were found in terms of gender or ethnicity. Apart from hypertension, cardiovascular risk factors were similar in both groups. To detect other factors confounding the effect of physical activity on mortality, other factors associated with prognosis in COVID-19 infection were analysed using univariate Cox regression. It showed that sedentary lifestyle, smoking habit, age and kidney disease were independent factors increasing the risk of death in patients infected with SARS-CoV-2. However, sedentary lifestyle, a modifiable factor, and age, a non-modifiable factor, had the highest confidence interval. It turned out that, despite similar symptoms on admission in both groups, the outcome during hospitalisation of patients with a sedentary lifestyle had a worse prognosis. Patients who were less active before hospitalisation, i.e. in group 1, were significantly more likely to develop generalised uncontrolled inflammatory response syndrome, SIRS (Systemic Inflammatory Response Syndrome), respiratory failure and renal failure, resulting in longer hospitalisation for this group of patients. Overall mortality was higher in patients with a sedentary lifestyle, and he was an independent predictor of mortality, confirmed by multivariate Cox regression analysis. Patients in group 2 who regularly undertook moderate-intensity physical activity prior to hospitalisation had better respiratory capacity and reserve than group 1, resulting in better compensatory capacity during SARS-CoV-2 infection. Mortality analysis showed an 8-fold higher risk of death in group 1 compared

with group 2. This study demonstrates that regular moderate to vigorous physical activity reduces mortality associated with SARS-CoV-2 infection. The group of patients with moderate, regular physical activity prior to hospitalisation tended to have higher haemoglobin oxygen saturation on admission and a lower incidence of respiratory failure despite a similar severity of pneumonia on X-ray, and therefore had greater resistance to hypoxaemia. Exercise decreases baseline minute ventilation and therefore increases oxygen uptake during exercise[35], resulting in greater resistance to hypoxaemia in group 2 patients.

Physical activity and risk of hospitalization and death

A cross-sectional study from January 2021 [36] investigated the severity of COVID-19 in athletes with regular sports participation in comparison to non-athletes. Patients from a hospital in Iran with subjective and physical symptoms of SARS-CoV-2 infection were recruited between 20 February and 20 April 2020. A total of 4694 adult patients were enrolled in the study, of whom 249 were involved in various sports. Only 12% (30 subjects) of the athletes were hospitalised or died, and the risk of hospitalisation was 33% lower than in patients who had no sport in their lives before admission. Mortality in this group reached 21.5%(957). This study shows that, irrespective of factors such as age and gender, regular participation in sport prior to COVID-19 was associated with a lower risk of hospitalisation and thus a lighter disease course.

The US Centers for Disease Control and Prevention (CDC)recommends at least 150 minutes of weekly activity of at least moderate intensity for all adults [42]. Restrictions imposed due to the COVID-19 pandemic have disallowed access to gyms, parks and other places where the public can be active. In a retrospective observational study in March 2021[37], researchers tried to determine whether consistent following of physical activity guidelines, before the diagnosis of COVID-19 was associated with a milder course of COVID-19 among infected adults. For this study, they used the record from the Electronic Health Record (EHR) of Southern California citizens, on which physical activity assessment data were recorded. This was done by asking 2 questions - about intensity and duration on a minimum of 3 visits made between 19 March 2018 and 18 March 2020. Inclusion criteria were being 18 years of age or older and receiving a positive PCR result for SARS-CoV-2 infection between 1 January 2020 and 21 October 2020. A total of 48,440 patients were included in the study. They were divided into 3 categories according to self-reported physical activity:

consistently inactive = 0-10 min of PA (physical activity)/week
some activity = 11-149 min of PA/week
consistently meeting guidelines=150+ min/week

8.6% of them were hospitalised, 2.4% were admitted to the Intensive Care Unit and 1.6% died. In order to better understand the data being compared, the results are presented in a table:

	consistently inactive	active but not achieving the recommended 150 minutes of moderate physical activity per week
Risk of hospitalisation	2,26 – fold higher	1,89- fold higher
ICU admission	1,73- fold higher	1,58- fold higher
death after COVID-19 diagnosis	2,49- fold higher	1,88- fold higher

Continued inactivity increased the risk of hospitalisation by 2.26 - fold compared with those meeting CDC guidelines. Those active but not achieving the recommended 150 minutes of moderate physical activity per week had a 1.89-fold increased risk of hospitalisation compared with those meeting CDC guidelines. The risk of ICU admission was 1.73 fold higher in those who were inactive and 1.58 fold higher in those who were active but did not meet the criteria of 150 minutes of moderate-intensity exercise per week, compared with the group of people who were sporting according to CDC guidelines. Mortality, on the other hand, was 2.49-fold higher in the first group and 1.88-fold higher in the second group, respectively, compared to those meeting the US CDC physical activity guidelines. Furthermore, in each of the factors compared - hospitalisation, ICU (Intensive Care Unit) admission or mortality - those who were not physically active were at higher risk compared to those who were active but did not meet the CDC guidelines. This study indicates that 150 minutes of moderate-intensity weekly activity was a strong protective factor against severe COVID-19 among infected adults. It is relevant to mention that physical inactivity was one of the stronger risk factors for severe COVID-19 infections compared to factors commonly cited, i.e. smoking, obesity, diabetes, hypertension, cardiovascular disease, and cancers[38].

Physical activity and risk of SARS-CoV-2 infection in patients with metabolic diseases.

A retrospective community-based cohort study in Korea was conducted to investigate the association of physical activity with morbidity and mortality resulting from SARS-CoV-2 infection in South Korea [39]. Patients who were 18 years of age or older, had a positive PCR test for SARS-CoV-2 (throat and nasal swab) between 1 January and 16 July 2016, and underwent public health screening between 2014 and 2017 were included in the study. The study group accounted for a total of 6288 individuals. The control group, matched for age and gender, was randomly selected from the database of the Korean National Health Insurance Service. The control group consisted of 125,772 individuals. Patients, in the study group, had a higher BMI and were more likely to have diabetes and obesity than patients in the control group. Hypertension was more common in patients in the control group. Screening included taking a medical history, anthropometric measurements and biochemical laboratory tests. Leisure-time activity was assessed using a self-completed questionnaire. The questionnaire divided the group of subjects according to the intensity of physical activity performed:

- light intensity: walking at own pace at slow speed

- moderate intensity: brisk walking, playing tennis, or slow cycling

- vigorous intensity: running, jogging, climbing, or bicycling or fast cycling

The different categories received scores of 2.9, 4.0, 7.0 on the MET (Metabolic Equivalent of Tasks) scale, respectively. The MET scale is used to assess exercise intensity. MET is the ratio of work metabolic rate (energy consumption during a specific physical activity) to rest metabolic rate (energy consumption during sleep)[40]. The subjects' energy expenditure was calculated by adding the frequency (number of days on which sport was played out of the last seven, for at least 30 min) and intensity of physical activity, measured on the MET scale. Physical activity level was grouped according to energy expenditure into:

totally sedentary or physical inactivity = 0 MET-min/week
physical activity < 500 MET-min/week
500 ≤ physical activity < 1000 MET-min/week

1000 ≤ physical activity < 1500 MET-min/week
physical activity ≥ 1500 MET-min/week

The mean level of physical activity in all patients was 579.1 ± 525.3 MET-min/week. MVPA (Moderate to Vigorous Physical Activity) is the amount of time a patient spent in above-moderate activity. This term was created for the US Centers for Disease Control and Prevention, which recommends a minimum of 150 minutes of moderate physical activity per week. It is defined in terms of percentage, time and average per day. MVPA was shorter in patients in the study group than in the control group, and this result was highly statistically significant. Central obesity significantly influenced the effect of physical activity on the risk of Covid-19. The beneficial effect of physical activity was more significant in centrally obese than in lean subjects. However, age, general obesity, hypertension and diabetes did not modify the effect of physical fitness on the risk of COVID-19. MVPA was associated with a 10% lower risk of SARS-CoV-2 infection and a 53% lower risk of mortality associated with COVID-19 infection, regardless of confounding factors. The highest level of physical activity (≥1500 MET-min/week) was associated with a 25% and 77% lower risk of COVID-19 infection and lower mortality, respectively, compared with the physically inactive group. In the study presented above, it was MVPA , rather than light physical activity, that was correlated with the lowest risk of infection and a 62% lower risk of COVID-19 mortality, supporting the notion that physical activity of moderate or higher intensity may have an additional beneficial effect on the prevention of COVID-19 infection. The anti-metabolic and anti-inflammatory effects of physical activity may explain the strong benefits experienced by obese individuals. In this study, central obesity, but not general obesity, significantly increased the beneficial effects of physical activity. This result supports the view that people with central obesity should be encouraged to be physically active.

CONCLUSION:

The abovementioned review indicates a protective effect of regular physical activity on the severity of COVID -19 infection, including hospitalisation, admission to the Intensive Care Unit or death. Regular physical activity before illness was associated with higher vital lung capacity, and better oxygen reserve, which was protective against hypoxaemia. Physical activity is a modifiable factor in reducing morbidity and the risk of severe SARS-CoV-2, so authorities

should consider whether imposing restrictions that were associated with reduced physical activity would do more good than harm. Prioritising physical activity higher among pandemic control methods may be a simple precaution against the high risk of mortality during the coming pandemic waves.

DISCLOSURE

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