



# The Evaluation of Physiopathological and Immunological Exercise Effects During Pandemic and Pathogenicity on Coronavirus COVID-19 (with Considerations and Instructions of Doing Related Physical Activity)

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Received 2024 April 14; Accepted 2024 April 30.

## Abstract

**Context:** The 2019 coronavirus disease (COVID-19), also commonly known as the coronavirus, is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is associated with several challenges, including an increased sedentary lifestyle, obesity, and elevated inflammatory factors and related diseases.

**Evidence Acquisition:** In conducting this research, we utilized the latest articles from prestigious domestic and foreign journals indexed in databases such as PubMed, Google Scholar, and ScienceDirect.

**Results:** There are various hypotheses regarding the intensity of exercise and its impact on infection rates. Moderate-intensity exercise is believed to enhance immune function and reduce mortality, whereas high-intensity and stressful exercise may have the opposite effect. When exposed to infection, high-intensity exercise can suppress the immune system, whereas moderate-intensity exercise may reduce inflammation.

**Conclusions:** Therefore, given that exercise affects the strength and anti-inflammatory mechanisms of the immune system, it plays a crucial role in reducing complications for patients. Consequently, it can be concluded that exercise strengthens the immune system, reduces inflammation, and creates favorable physiological and immunological conditions to aid athletes in overcoming the virus.

**Keywords:** COVID-19, Physiopathology, Immunology, Exercise, Pandemic

## 1. Context

MERS is now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). When a person infected with the virus sneezes or coughs into the air or onto a surface, the virus enters the host's body through the mouth, nose, or eyes. Among the challenges associated with this disease are increased inactivity, obesity, and a rise in inflammatory factors and related diseases (2). Conversely, both the World Health Organization (WHO) and the Ministry of Health have mandated home quarantine measures for affected countries. Accordingly, a fundamental question arises: Are individuals permitted to engage in sports activities

during these epidemic conditions to maintain minimal physical fitness? If exercise is deemed safe for some individuals during a coronavirus outbreak, what are the recommended practices (3)? To date, there has been limited scientific research on the coronavirus, particularly concerning the effects of exercise and physical activity on its various dimensions. However, based on the physiological characteristics of the coronavirus and its impact on the immune system, this article aims to address these issues by reviewing previous research on the effects of exercise on the immune system in other viral diseases, along with existing sports recommendations. Moreover, specific sports guidelines for various groups should be established to offer scientific insights for sports

professionals, coaches, and the general public during periods of home quarantine and social distancing (2).

## 2. Evidence Acquisition

This study belongs to the category of secondary research, employing a methodology focused on reviewing the most pertinent sources available. The examination of sources occurred within the specific timeframe from January 2019 to November 2020. During this investigation, the latest Persian and English articles from reputable domestic and international journals, as well as those indexed in databases such as PubMed, Google Scholar, Science Direct, WHO, etc., were scrutinized (4, 5). Among these articles, those most relevant to the impact of COVID-19 on exercise physiopathology were selected for thorough review and analysis.

The study falls under the classification of secondary research, wherein the latest Persian and English articles from reliable domestic and international scientific databases and journals were surveyed. This process involved databases such as PubMed (American medical science database), ACSM (American college of sports medicine), Science Direct, Google Scholar, and Elsevier publications. The search spanned from 2010 to 2022, resulting in the identification of 42 articles. Subsequently, 15 articles that did not align with the research objectives were excluded, leaving 27 articles for analysis. Criteria for inclusion in the study encompassed topical relevance, novelty, inclusion of non-athletes in the studied population, and the intervention of various types of sports training in the prevention or amelioration of diverse complications. Following a meticulous review process utilizing standardized templates, the abstracts and relevant sections of the selected studies were categorized and subjected to content analysis.

Among the identified articles, those most pertinent to the effects of COVID-19 on sports physiopathology were singled out. Additionally, indicators such as topical relevance, novelty, inclusion of non-athletes in the studied population, and the intervention of various types of sports training in the prevention or amelioration of various complications were employed as criteria for the inclusion of articles in this study. The findings of the selected texts were subsequently subjected to further analysis (figure 1).

## 3. Results

The COVID-19 pandemic and its impact on the immune and respiratory systems have raised many

questions about how exercise can protect our bodies against viral infections by boosting immunity. Inactivity increases the risk of type 2 diabetes (6), cardiovascular diseases (7), various cancers (8, 9), depression (10), and increased subcutaneous fat (11). Conversely, the anti-inflammatory effects of sports activities on diseases related to chronic inflammation are well-documented (12). During periods of inactivity, an increase in glucocorticoids such as cortisol weakens the immune system, significantly reducing the ability of T cells to proliferate in response to infectious agents (13). In contrast, each exercise session, especially dynamic cardiorespiratory activities, rapidly mobilizes billions of immune cells, notably those capable of performing crucial functions such as identifying and killing virus-infected cells (13). Among these functions is the release of anti-inflammatory cytokines, which help maintain immunity and enhance the body's resistance to infection (14). Some research findings suggest that exercise offers protection against viruses such as influenza, rhinovirus, and herpesviruses, including Epstein-Barr, varicella-zoster, and herpes simplex virus type 1 (14, 15). However, the type of exercise is important. It has been demonstrated that moderate-intensity exercise during active influenza infection prevents death in mice, maintains better immune cell structure, and alters lung cytokines, ultimately leading to greater survival in rats (16). Moderate-intensity training increases the immune response to vaccines and reduces exhausted T cells (17). Conversely, increasing the proliferation of T cells results in a decrease in inflammatory cytokines such as IL2 (17, 18). One of the most prominent complications of coronavirus disease is an increase in inflammation and inflammatory markers, including C-reactive protein. However, different types of exercise can reduce both inflammation and inflammatory markers (19, 20). Various hypotheses exist about the intensity of exercise and the rate of infection, including hypothesis J. This hypothesis illustrates the relationship between the risk of upper respiratory tract infection and the level of physical activity, as shown in Figure 2.

The J-curve is a concept that describes the relationship between the amount of physical activity and the risk of cardiovascular diseases. It suggests that the risk of cardiovascular diseases is higher in people who engage in very little or excessive physical activity, and lower in those who engage in moderate physical activity.

This concept originates from many researches in the field of physical activity and health. Some studies show that moderate intensity exercise can reduce the risk of

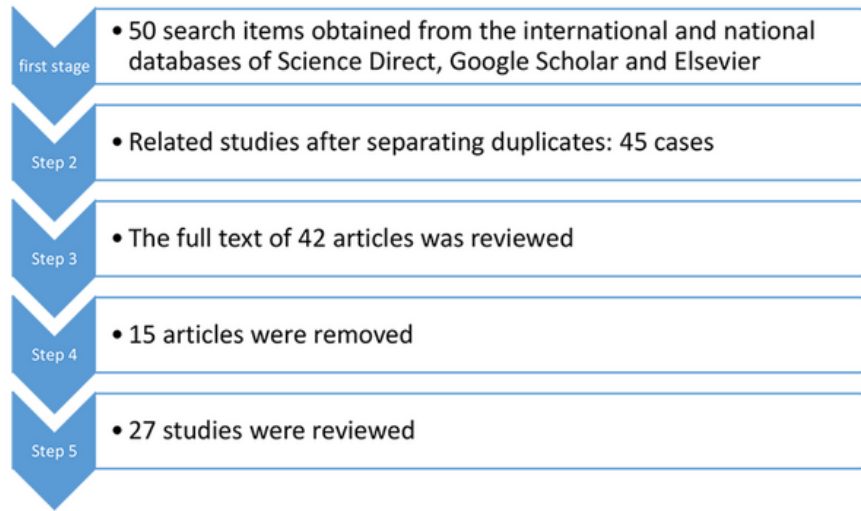


Figure 1. Flowchart of reviewed articles

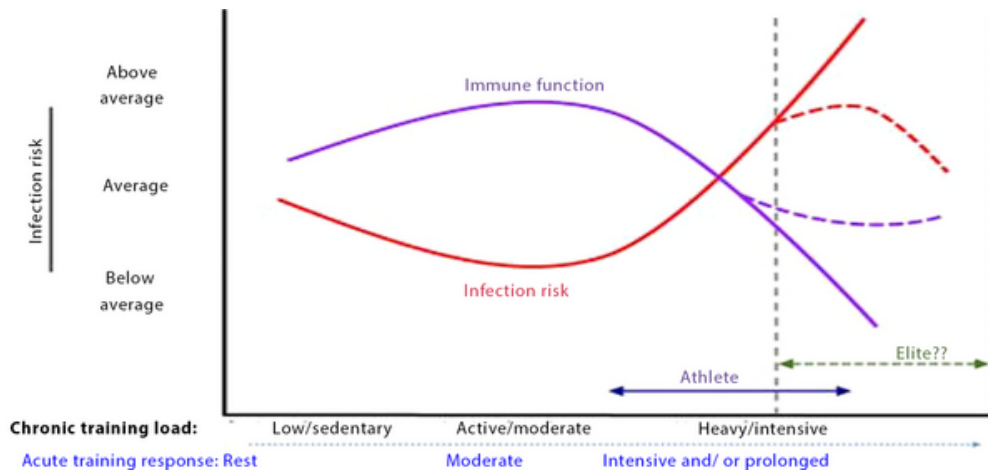


Figure 2. Curve-J, relationship between exercise intensity and risk of infectious diseases

cardiovascular diseases and other chronic diseases such as diabetes, respiratory disease, cancer, and increases life expectancy.

Therefore, it can be said that this concept originates from many researches in the field of physical activity and health, and it shows that the risk of cardiovascular diseases is higher in people who have too little or too much physical activity. Therefore, in order to maintain good health, it is recommended to keep your physical

activity at a moderate level that contributes to good health.

Research indicates that moderate-intensity physical activity improves immune system function and reduces mortality (21), while high-intensity and stressful exercise can have the opposite effect (22). Epidemiological studies suggest that high-intensity and competitive exercise increases susceptibility to upper respiratory

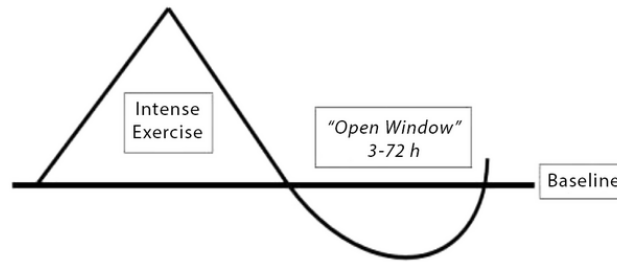


Figure 3. Open window hypothesis: Decreased immune function 3 to 72 hours after strenuous exercise

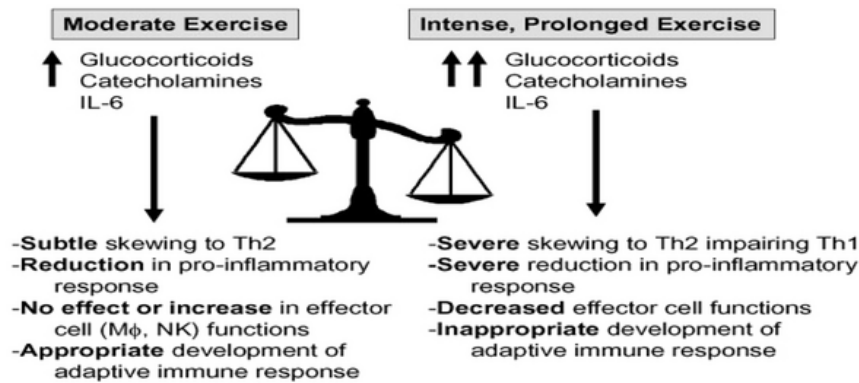


Figure 4. A model for describing the effect of dose-response of exercise activity on Th1 and Th2 (27)

tract infections, whereas gentle physical activity may reduce the symptoms of these infections (23).

The J-curve illustrates that individuals experiencing mild symptoms of upper respiratory tract infections can engage in exercise, whereas those with severe sore throat, body aches, shortness of breath, general fatigue, dry cough, or fever should avoid physical activity. Recovery from viral infections generally requires 2 to 3 weeks of rest. Once symptoms have completely subsided, engaging in light sports activities is considered safe (24, 25).

#### 4. Conclusions

Performing intense and stressful activities suppresses immune parameters, while moderate-intensity exercise reduces inflammation and respiratory viral infections (25). Some studies demonstrate the relationship between regular sports activities and the reduction of influenza and pneumonia incidence (26). It

is advisable to limit sports activities during respiratory tract infections because, according to the open window hypothesis, engaging in high-intensity sports activities increases susceptibility to infection in untrained individuals (Figure 3). According to this hypothesis, the immune system's function decreases 3 to 72 hours after intense exercise. Moderate-intensity exercise causes a relative increase in catecholamines, IL6, and glucocorticoids, along with a slight increase in the ratio of Th1 to Th2, ultimately enhancing adaptive immune responses. Conversely, intense and prolonged exercise leads to a further increase in catecholamines, IL6, and glucocorticoids, disrupting adaptive immune responses (Figure 4).

Based on research regarding the intensity of sports activities and TH1 and TH2 immune responses to respiratory virus infections, it can be concluded that healthy and asymptomatic individuals can engage in moderate-intensity exercises following health protocols

(27). Although studies on the effects of regular exercise specifically on this disease have not yet been published due to the novelty of COVID-19, previous research on the effects of physical activity on immune system function and similar viral diseases like influenza suggests that regular exercise and an active lifestyle, by increasing energy expenditure and improving physical and mental fitness, promote health and reduce the likelihood of viral infections. In the event of COVID-19 infection, regular exercise can aid in recovery. Considering that both interval and resistance training have significant impacts on cardiorespiratory endurance and muscle strength, respectively, a combination of these activities is recommended to enhance overall health and fitness. Additionally, recognizing that different age and social groups respond differently to COVID-19 and sports activities, prescribing sports activities tailored to specific guidelines for each group is advisable to prevent further harm and risks.

## Acknowledgements

The authors declare that there was no financial support.

## Footnotes

**Authors' Contribution:** AA compilation and writing of the article ;SAA editing the article ;MBN supervisor and editor ;all authors read and approved the final manuscript.

**Conflict of Interests:** The authors declare that there are no conflicts of interest.

**Data Reproducibility:** It was not declared by the authors.

**Funding/Support:** It was not declared by the authors.

## References

- Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbutto V, Veronese N, et al. Coronavirus Diseases (COVID-19) Current Status and Future Perspectives: A Narrative Review. *Int J Environ Res Public Health*. 2020;**17**(8). [PubMed ID: 32295188]. [PubMed Central ID: PMC7215977]. <https://doi.org/10.3390/ijerph17082690>.
- Ahmadizad S, Basami M. [Exercise role in improving the immune system and physical fitness during Corona pandemic period and associated exercise guidelines]. *J Sport Exerc Physiol*. 2020;**13**(1):1-15. Persian. <https://doi.org/10.52547/joeppa.13.1.1>.
- Shirvani H, Rostamkhani F. [Exercise Considerations During Coronavirus Disease (COVID-19) Outbreak: A Narrative Review]. *J Military Med*. 2020;**22**(2):161-8. Persian.
- Hamidi Parchiklaei SO, Hashemvarzi SA. A review article on the physiological and immunological effects of exercise training on the pathogenesis of coronavirus 2019 COVID-19. Tehran, Iran. The 6th National Conference of Sports Sciences and Physical Education of Iran; 2019.
- World Health Organization. *World Health Organization*. Geneva, Switzerland: World Health Organization; 2020, [cited 2023]. Available from: <https://www.who.int/>.
- Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;**344**(18):1343-50. [PubMed ID: 11333990]. <https://doi.org/10.1056/NEJM200105033441801>.
- Nocon M, Hiemann T, Muller-Riemenschneider F, Thalau F, Roll S, Willich SN. Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. *Eur J Cardiovasc Prev Rehabil*. 2008;**15**(3):239-46. [PubMed ID: 18525377]. <https://doi.org/10.1097/HJR.0b013e3282f55e09>.
- Monninkhof EM, Elias SG, Vleems FA, van der Tweel I, Schuit AJ, Voskuil DW, et al. Physical activity and breast cancer: a systematic review. *Epidemiol*. 2007;**18**(1):137-57. [PubMed ID: 17130685]. <https://doi.org/10.1097/01.ede.0000251167.75581.98>.
- Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer*. 2009;**100**(4):611-6. [PubMed ID: 19209175]. [PubMed Central ID: PMC2653744]. <https://doi.org/10.1038/sj.bjc.6604917>.
- Paffenbarger RJ, Lee IM, Leung R. Physical activity and personal characteristics associated with depression and suicide in American college men. *Acta Psychiatr Scand Suppl*. 1994;**377**:16-22. [PubMed ID: 8053361]. <https://doi.org/10.1111/j.1600-0447.1994.tb05796.x>.
- Pedersen BK. The disease of physical inactivity--and the role of myokines in muscle-fat cross talk. *J Physiol*. 2009;**587**(Pt 23):5559-68. [PubMed ID: 19752112]. [PubMed Central ID: PMC2805368]. <https://doi.org/10.1113/jphysiol.2009.179515>.
- Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol (1985)*. 2005;**98**(4):1154-62. [PubMed ID: 15772055]. <https://doi.org/10.1152/japplphysiol.00164.2004>.
- Walsh NP, Gleeson M, Pyne DB, Nieman DC, Dhabhar FS, Shephard RJ, et al. Position statement. Part two: Maintaining immune health. *Exerc Immunol Rev*. 2011;**17**:64-103. [PubMed ID: 21446353].
- Walsh NP, Gleeson M, Shephard RJ, Gleeson M, Woods JA, Bishop NC, et al. Position statement. Part one: Immune function and exercise. *Exerc Immunol Rev*. 2011;**17**:6-63. [PubMed ID: 21446352].
- Simpson RJ, Kunz H, Agha N, Graff R. Exercise and the Regulation of Immune Functions. *Prog Mol Biol Transl Sci*. 2015;**135**:355-80. [PubMed ID: 26477922]. <https://doi.org/10.1016/bs.pmbts.2015.08.001>.
- Lowder T, Padgett DA, Woods JA. Moderate exercise protects mice from death due to influenza virus. *Brain Behav Immun*. 2005;**19**(5):377-80. [PubMed ID: 15922557]. <https://doi.org/10.1016/j.bbi.2005.04.002>.
- Spielmann G, McFarlin BK, O'Connor DP, Smith PJ, Pircher H, Simpson RJ. Aerobic fitness is associated with lower proportions of senescent blood T-cells in man. *Brain Behav Immun*. 2011;**25**(8):1521-9. [PubMed ID: 21784146]. <https://doi.org/10.1016/j.bbi.2011.07.226>.
- Drela N, Kozdron E, Szczypiorski P. Moderate exercise may attenuate some aspects of immunosenescence. *BMC Geriatr*. 2004;**4**:8. [PubMed ID: 15456521]. [PubMed Central ID: PMC524506]. <https://doi.org/10.1186/1471-2318-4-8>.
- Ahmadizad S, Avansar AS, Ebrahim K, Avandi M, Ghasemikaram M. The effects of short-term high-intensity interval training vs. moderate-intensity continuous training on plasma levels of nesfat-1 and inflammatory markers. *Horm Mol Biol Clin Invest*. 2015;**21**(3):165-73. [PubMed ID: 25581765]. <https://doi.org/10.1515/hmbci-2014-0038>.

20. Hovanloo F, Arefirad T, Ahmadizad S. Effects of sprint interval and continuous endurance training on serum levels of inflammatory biomarkers. *J Diabetes Metab Disord*. 2013;**12**(1):22. [PubMed ID: 23725447]. [PubMed Central ID: PMC3674904]. <https://doi.org/10.1186/2251-6581-12-22>.
21. Nieman DC, Nehlsen-Cannarella SL. The immune response to exercise. *Semin Hematol*. 1994;**31**(2):166-79. [PubMed ID: 8066473].
22. Brown AS, Davis JM, Murphy EA, Carmichael MD, Ghaffar A, Mayer EP. Gender differences in viral infection after repeated exercise stress. *Med Sci Sports Exerc*. 2004;**36**(8):1290-5. [PubMed ID: 15292734]. <https://doi.org/10.1249/01.mss.0000135798.72735.b3>.
23. Wong CM, Lai HK, Ou CQ, Ho SY, Chan KP, Thach TQ, et al. Is exercise protective against influenza-associated mortality? *PLoS One*. 2008;**3**(5). e2108. [PubMed ID: 18461130]. [PubMed Central ID: PMC2329855]. <https://doi.org/10.1371/journal.pone.0002108>.
24. Zhu W. Should, and how can, exercise be done during a coronavirus outbreak? An interview with Dr. Jeffrey A. Woods. *J Sport Health Sci*. 2020;**9**(2):105-7. [PubMed ID: 32099717]. [PubMed Central ID: PMC7031769]. <https://doi.org/10.1016/j.jshs.2020.01.005>.
25. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. *J Sport Health Sci*. 2019;**8**(3):201-17. [PubMed ID: 31193280]. [PubMed Central ID: PMC6523821]. <https://doi.org/10.1016/j.jshs.2018.09.009>.
26. Sim YJ, Yu S, Yoon KJ, Loiacono CM, Kohut ML. Chronic exercise reduces illness severity, decreases viral load, and results in greater anti-inflammatory effects than acute exercise during influenza infection. *J Infect Dis*. 2009;**200**(9):1434-42. [PubMed ID: 19811098]. [PubMed Central ID: PMC2812897]. <https://doi.org/10.1086/606014>.
27. Martin SA, Pence BD, Woods JA. Exercise and respiratory tract viral infections. *Exerc Sport Sci Rev*. 2009;**37**(4):157-64. [PubMed ID: 19955864]. [PubMed Central ID: PMC2803113]. <https://doi.org/10.1097/JES.0b013e3181b7b57b>.