Review Article

Can exercise be used as a protective agent against disease severity in COVID-19 and as treatment during subsequent rehabilitation?

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ABSTRACT

In a matter of months, COVID-19 has spread worldwide, and it has affected not only human lives but also the socioeconomic structure. Disease severity increases with the presence of other factors such as age, diabetes, and hypertension. Exercise has been shown to control blood pressure and blood sugar level; it enhances the immune system and age-related physiological changes. Given its ability to control all of these factors, exercise can be used as a protective agent against disease severity in COVID-19 and as treatment during subsequent rehabilitation.

Key words: COVID-19; severity; exercise; hypertension; diabetes; age; rehabilitation; physical therapy.

RESUMEN

En cuestión de meses la COVID-19 se ha expandido a todo el mundo y su impacto no solo ha sido en vidas humanas, sino también en la estructura socioeconómica. La severidad de la enfermedad aumenta en presencia de factores tales como edad, diabetes e hipertensión. Se ha demostrado que el ejercicio puede controlar la presión sanguínea y los niveles de azúcar en sangre, además de aumentar la función inmune y cambios fisiológicos relacionados con la edad. Dada a la habilidad de controlar todos estos factores, el ejercicio tiene el potencial de ser usado como factor protector para reducir la severidad de la COVID-19 y como tratamiento durante la rehabilitación subsecuente.

Palabras clave: COVID-19; severidad; ejercicio; hipertensión; diabetes; edad; rehabilitación; terapia física.

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1. INTRODUCTION

Since its first appearance in December 2019, COVID-19 has spread from its place of origin in China to the whole world in months. It has an incubation period of 5 days and has symptoms like fever, dry cough, and fatigue.[1] The main form of transmission is via droplets, and it can affect several tissues besides the lungs, such as the central nervous system, heart, liver, gastrointestinal tract, and kidneys.[2] The most common risk factors for disease severity for COVID-19 are diabetes, age, and hypertension.[3–6] Until now, there is no known cure, and the best strategy for controlling its spread has been the implementation of preventive measures, such as social distancing, use of face masks, quarantine, the proper cleaning of surfaces, and hand washing.[7] COVID-19 has had an impact on every aspect of the world socioeconomic landscape and is estimated to have long-term repercussions.[8]

Benefits of physical activity have been well documented, from a better quality of sleep, anxiety and weight management, and lower cardiovascular disease risk to reduction of all-cause mortality, among others.[9–12] The terms physical activity and exercise are sometimes used interchangeably, but one should not be confused with the other. Exercise must be a planned, structured, repetitive, and purposeful physical activity with measurement methods.[13] Zbinden-Foncea, Deldicque, and Howley reviewed the possible role of exercise as a preventive strategy to decrease the severity of COVID-19, focusing on its role in regulating the inflammatory status.[14] This review will focus on the role of exercise during the COVID-19 pandemic, from reducing risk factors for disease severity to its role during rehabilitation in disease recovery.

2. SUBTOPICS

Blood pressure control

Although hypertension is considered a risk factor for COVID-19 severity[15,16], the changes in the pro-inflammatory status and immune suppression that accompany hypertension are the reason why it is considered a risk factor.[17] Nevertheless, data suggests that patients with poor blood pressure control have higher rates of adverse outcomes like mortality, ICU admission, heart failure, respiratory failure, and mechanical ventilation.[18–19] One possible treatment line for preventing adverse outcomes in these patients is to keep blood pressure under control. After an acute bout of exercise, there is a decrease in blood pressure known as post-exercise hypotension (PEH). There are several mechanisms for this change in pressure, and it is likely a combination of neural and hormonal mechanisms.[20–22] One strong candidate for PEH is post-exercise baroreflex. After exercise cessation, there is an increased sympathetic nervous activity that causes a reset in the baroreflex, thus decreasing blood pressure.[23,24] As little as 30−60 min aerobic exercise per week is enough to lower blood pressure.[25] Even in resistant hypertension, interval walking exercise decreases blood pressure.[26] Thirty minutes of moderate treadmill walking lowers systolic and diastolic blood pressure over 8 hours of prolonged sitting.[27] Aerobic exercise in the evening results in a better hypotensive effect when compared to exercise done in the morning in hypertensive individuals, although both options are effective in lowering blood pressure.[27] High-Intensity Interval Training (HIIT) can provide a longer[28] or the same[29] hypotensive effect as continuous aerobic exercise. Isometric handgrip has been proposed as a cost-effective, low-equity alternative to decrease blood pressure.[30–32] However, aerobic exercise yields a better blood pressure control response when compared with isometric exercise.[33,34]

Glycemic control

It has been hypothesized that people with diabetes appear to have worse outcomes because of high levels of blood glucose and changes in their physiology that accompany diabetes. Among these changes are increased ACE-2 expression and furin levels, impaired T cell function, increased interleukin-6 (IL-6) levels, and impaired neutrophil chemotaxis and phagocytosis.[15,35,36] In a cohort of 7,337 patients with confirmed COVID-19 and type-2 diabetes, individuals who had well-controlled glucose levels (6.4 mmol/L) had a higher lymphocyte count and lower neutrophil and serum IL-6 levels. Furthermore, they had reduced organ injury and lower death rates compared to patients with poorly controlled glucose levels.[37] It could be argued that a possible prevention strategy for the diabetic patient is to keep their blood glucose under control. Glycemic control (GC) refers to the regulation of glucose that a human has in their system. The mechanisms of GC as a response to exercise are a combination of increased blood flow, permeability, and glucose requirements during exercise.[38] Exercise is a recommended lifestyle change for GC in individuals with type-1 and type-2 diabetes.[39,40] Resistance and aerobic exercise decrease glucose in type-1 diabetes; resistance exercise decrease mean glucose for 24 hours post-exercise.[41] Both continuous and interval aerobic exercises result in decreased glucose in type 2 diabetes.[42] Even walking exercise programs can be useful in decreasing glucose levels. An interval-style walking program resulted in decreased mean and maximum glucose concentration compared to continuous walking.[43] Exercise can also be used as a prevention strategy for the development of type-2 diabetes. HIIT has been shown to prevent the progression of type-2 diabetes in prediabetic individuals.[44]

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Exercise as a countermeasure for age-related physiological changes

Aging is related to a series of changes that affect all systems within the human body. These changes comprise an increase in arterial wall stiffness [45], a decrease in muscle strength, size, bone mineral density (BMD)[46] and lung structure, which affects gas exchange [47], and a decrease in immune cell count and function[48], among others. All these changes lead the individual to a state known as frailty [49-52] and it appears that these changes in which the organism is unable to adapt and maintain homeostasis is the reason why the elderly are amongst the at-risk population [53,54]. One possible alternative to manage this population is to prevent these changes from happening altogether. The direct connection between aerobic exercise and longevity has been shown in animal studies. The survival chances increased ~25% when the animal had higher VO2max while doing aerobic exercise, lowering cholesterol levels and arterial pressure and increasing glucose tolerance, alveolar ventilation, and pulmonary diffusion.[55,56] Exercise can improve cardiorespiratory function through various mechanisms such as an increase in muscle mass and heart function.[57] High and low-intensity resistance exercise leads to improved oxygen consumption and cardiorespiratory endurance.[58] Aerobic and endurance exercise, coupled with interval training, produced an increase in VO2max and skeletal muscle area and strength.[59] A combination of aerobic and resistance exercise leads to increased muscle strength and body composition changes in sarcopenic obese individuals.[60] A cross-sectional study showed that men who performed moderate-to-vigorous exercise showed a lower risk of osteoporosis.[61] A 5-month resistance and aerobic exercise intervention effectively reduced BMD loss during caloric restriction in older adults, although resistance exercise showed better results.[62] Resistance exercise can improve muscle size, quality, and power production as well as physical function in older adults.[63] Both supervised and home-based exercise improved lower limb strength and walking speed in frail and pre-frail individuals.[64] Changes in immune parameters can still be obtained despite age. Master athletes exhibited lower senescent lymphocytes compared to healthy age-matched controls.[65] The aerobic exercise yielded a better immune response than resistance exercise in the elderly.[66] Both acute and chronic exercise has a positive effect on immune parameters in the elderly.[67] Altogether, evidence supports the notion that the stimulus by exercise leads to changes in the physiology, specifically when it comes to blood pressure control, glycemic control, and the delay and even reversal of age related changes. This may confer some protection against COVID-19 severity.

Role of exercise in cardiopulmonary rehabilitation

The role of exercise in pulmonary rehabilitation has been well established, and rehabilitation can start as early as in the intensive care unit (ICU). Elastic bands have been used effectively and safely in the ICU to prevent a decline in upper body strength and trunk control.[68] Cycling combined with functional electric stimulation increased cardiac output in patients during bed stay at the ICU.[69] British Thoracic Society Guidelines places exercise as an integral part of pulmonary rehabilitation given that it enhances muscle size and function, pulmonary capacity, and residual capacity.[70] Exercise can also help regulate symptom control and quality of life. Moderate aerobic exercise resulted in better symptom control and quality of life in patients with chronic obstructive pulmonary disease (COPD).[71] Considering the COVID-19 lockdown, rehabilitation must be done in a home-based setting. Home-based telerehabilitation in individuals with COPD leads to

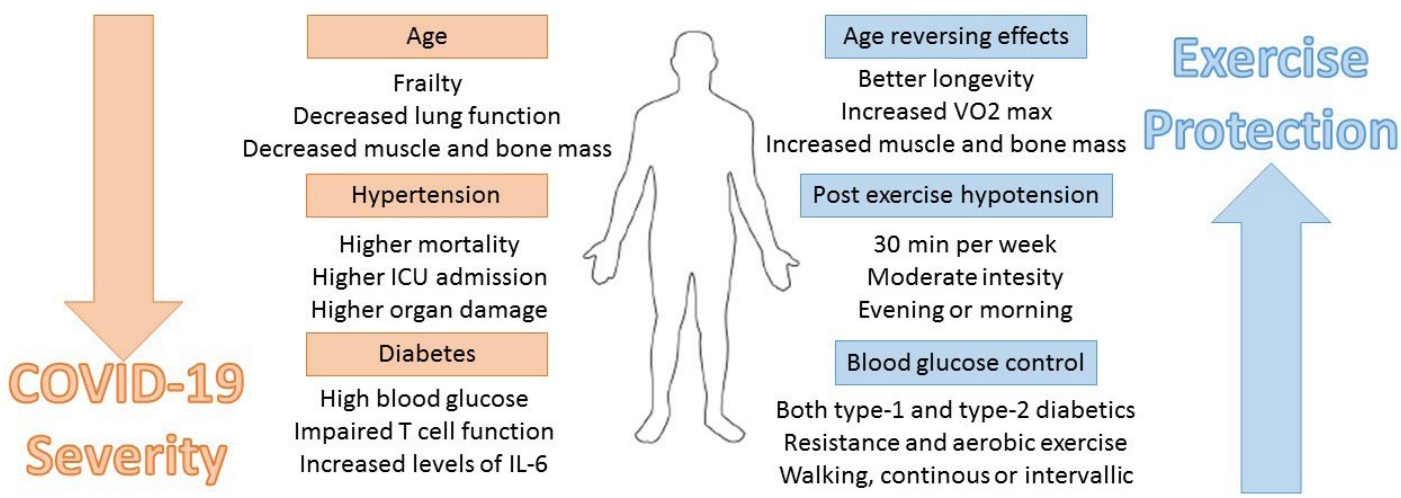

Figure 1. Relationship between exercise and COVID-19 risk factors.

increased exercise capacity and quality of life.[72] Six months of telerehabilitation with COPD and heart failure effectively reduced hospitalization rate, exercise tolerance measured by 6-minute walk test, increased quality of life, and reduced dyspnea.[73] Individuals undergoing home-based cardiac rehabilitation showed improvement in VO2max and quality of life.[74] Exercise can also provide a treatment option for non-disease side effects of the COVID-19 pandemic, such as mental exhaustion, depression, sedentarism, mood changes, self-esteem, and even social isolation.[75–77] Exercise can provide a viable treatment option for the rehabilitation of COVID-19 patients in every step of the way, from ICU stay to outpatient rehabilitation and even at-home exercise programs (Figure 1).

3. CONCLUSION

Exercise could be used as a low-cost treatment for reducing risk factors and mortality from COVID-19. HIIT appears to be a time-effective option to reduce COVID-19 disease severity factors. Several challenges need to be considered, such as a correct exercise prescription by a certified physical therapist. Therapy must be based on specific needs, abilities, and monitoring of the individual and equipment needed to ensure a correct and safe exercise execution, all while maintaining preventive measures against COVID-19.

4. CONFLICT OF INTERESTS

The authors declare no conflict of interest.

5. REFERENCES

1. Wu Y-C, Chen C-S, Chan Y-J. The outbreak of COVID-19: An overview. J Chinese Med Assoc. 2020;83:217–20.
https://doi.org/10.1097/JCMA.0000000000000270
2. Machhi J, Herskovitz J, Senan AM, Dutta D, Nath B, Oleynikov MD, et al. The Natural History, Pathobiology, and Clinical Manifestations of SARS-CoV-2 Infections. J Neuroimmune Pharmacol. 2020;15:359–86.
https://doi.org/10.1007/s11481-020-09944-5
3. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020;e3319.
https://doi.org/10.1002/dmrr.3319
4. Baradaran A, Ebrahimzadeh MH, Baradaran A, Amir, Kachooei R, Kachooei AR. SYSTEMATIC REVIEW Prevalence of Comorbidities in COVID-19 Patients: A Systematic Review and Meta-Analysis. Arch Bone Jt Surg. 2020;8:247–55.
https://doi.org/10.1016/j.ijid.2020.03.017
5. Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: A review of clinical data in China. 2020;188:111255.
https://doi.org/10.1016/j.mad.2020.111255
6. Oviedo-Trespalacios OI, Cortes-Ramirez JI. A brief-review of the risk factors for covid-19 severity. Rev. Saude Publica. 2020;54:60.
http://doi.org/10.11606/s1518-8787.2020054002481
7. Güner R, Hasanoğlu İ, Aktaş F. Covid-19: Prevention and control measures in community. Journal of Medical Sciences. 2020;50:571-77.
https://doi.org/10.3906/sag-2004-146
8. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. International Journal of Surgery. 78:185-93.
https://doi.org/10.1016/j.ijsu.2020.04.018
9. Kelley GA, Kelley KS. Exercise and sleep: a systematic review of previous meta-analyses. J Evid Based Med. 2017;10(1):26–36.
https://doi.org/10.1111/jebm.12236
10. Stubbs B, Vancampfort D, Rosenbaum S, Firth J, Cosco T, Veronese N, et al. An examination of the anxiolytic effects of exercise for people with anxiety and stress-related disorders: A meta-analysi.s Psychiatry Research. 2020;249:102–108.
https://doi.org/10.1016/j.psychres. 2016.12.020
11. Zhao M, Veeranki SP, Magnussen CG, Xi B. Recommended physical activity and all cause and cause specific mortality in US adults: Prospective cohort study. BMJ. 2020;370(1):2031.
http://doi.org/10.1136/bmj.m2031
12. Benefits of Physical Activity | Physical Activity | CDC.
https://www.cdc.gov/physicalactivity/basics/pa-health/index.htm
13. Dasso NA. How is exercise different from physical activity? A concept analysis. Nurs Forum. 2019;54(1):45–52.
http://doi.org/10.1111/nuf.12296
14. Zbinden-Foncea H, Francaux M, Deldicque L, Hawley JA. Does High Cardiorespiratory Fitness Confer Some Protection Against Proinflammatory Responses After Infection by SARS-CoV-2? Obesity. 2020;28(8):1378–81.
https://doi.org/10.1002/oby.22849
15. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr Clin Res Rev. 2020;14(4):303–10.
https://doi.org/10.1016/j.dsx.2020.04.004
16. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in

Wuhan. J Allergy Clin Immunol. 2020;146(1):110–8. https://doi.org/10.1016/j.jaci.2020.04.006

17. Kreutz R, Algharably EAEH, Azizi M, Dobrowolski P, Guzik T, Januszewicz A, et al. Hypertension, the renin-angiotensin system, and the risk of lower respiratory tract infections and lung injury: Implications for covid-19. Cardiovascular Research. 2020;16(10):1688–99. https://doi.org/10.1093/cvr/cvaa097
18. Ran J, Song Y, Zhuang Z, Han L, Zhao S, Cao P, et al. Blood pressure control and adverse outcomes of COVID-19 infection in patients with concomitant hypertension in Wuhan, China. Hypertens Res. 2020;43(11):1267–76. http://doi.org/10.1038/s41440-020-00541-w
19. Chen R, Yang J, Gao X, Ding X, Yang Y, Shen Y, et al. Influence of blood pressure control and application of renin-angiotensin aldosterone system inhibitors on the outcomes in COVID-19 patients with hypertension. J Clin Hypertens. 2020;22(11):1974-83. https://doi.org/10.1111/jch.14038
20. Chen CY, Bonham AC. Postexercise hypotension: Central mechanisms. Exerc Sport Sci Rev. 2010;38(3):122–7. https://doi.org/10.1097/JES.0b013e3181e372b5
21. Do Socorro Brasileiro-Santos M, Da Cruz Santos A. Neural mechanisms and post-exercise hypotension: The importance of experimental studies motriz. Revista de Educacao Fisica. 2017;23(1):e101622. https://doi.org/10.1590/s1980-6574201700si0006
22. Macdonald JR. Potential causes, mechanisms, and implications of post exercise hypotension. J Hum Hypertens. 2002;16(1): 225–36. https://doi.org/10.1038/sj.jhh.1001377
23. Miki K, Yoshimoto M. Exercise-induced modulation of baroreflex control of sympathetic nerve activity. Frontiers in Neuroscience. 2018;12(1):493. https://doi.org/10.3389/fnins.2018.00493
24. Oliveira R, Barker AR, Debras F, O'Doherty A, Williams CA. Mechanisms of blood pressure control following acute exercise in adolescents: Effects of exercise intensity on haemodynamics and baroreflex sensitivity. Exp Physiol. 2018;103(8):1056–66. https://doi.org/10.1113/EP086999
25. Ishikawa-Takata K, Ohta T, Tanaka H. How much exercise is required to reduce blood pressure in essential hypertensives: A dose-response study. Am J Hypertens. 2003;16(8):629–33. https://doi.org/10.1016/S0895-7061(03)00895-1
26. Dimeo F, Pagonas N, Seibert F, Arndt R, Zidek W, Westhoff TH. Aerobic exercise reduces blood pressure in resistant hypertension. Hypertension. 2012;60(3):653–8. https://doi.org/10.1161/HYPERTENSIONAHA.112.197780
27. Brito LC, Peçanha T, Fecchio RY, Rezende RA, Sousa P, Da Silva-Júnior N, et al. Morning versus Evening Aerobic Training Effects on Blood Pressure in Treated Hypertension. Med Sci Sports Exerc. 2019;51(4):653–62. https://doi.org/10.1249/MSS.0000000000001852
28. Maya ÁTD, Assunção MJ, Brito CJ, Vieira E, Rosa TS, Pereira FB, et al. High-intensity interval aerobic exercise induced a longer hypotensive effect when compared to continuous moderate. Sport Sci Health. 2018;14(2):379–85. https://doi.org/10.1007/s11332-018-0444-3
29. Gorostegi-Anduaga I, Corres P, MartinezAguirre-Betolaza A, Pérez-Asenjo J, Aispuru GR, Fryer SM, et al. Effects of different aerobic exercise programmes with nutritional intervention in sedentary adults with overweight/obesity and hypertension: EXERDIET-HTA study. Eur J Prev Cardiol. 2018;25(4):343–53. https://doi.org/10.1177%2F2047487317749956
30. McGowan CL, Proctor DN, Swaine I, Brook RD, Jackson EA, Levy PD. Isometric Handgrip as an Adjunct for Blood Pressure Control: a Primer for Clinicians. Current Hypertension Reports. 2017;19(1):51. https://doi.org/10.1007/s11906-017-0748-8
31. Van Assche T, Buys R, De Jaeger M, Coeckelberghs E, Cornelissen VA. One single bout of low-intensity isometric handgrip exercise reduces blood pressure in healthy pre- and hypertensive individuals. J Sports Med Phys Fitness. 2017;57(4):469–75. http://doi.org/10.23736/s0022-4707.16.06239-3
32. Badrov MB, Freeman SR, Zokvic MA, Millar PJ, McGowan CL. Isometric exercise training lowers resting blood pressure and improves local brachial artery flow-mediated dilation equally in men and women. Eur J Appl Physiol. 2016;116(7):1289–96. https://doi.org/10.1007/s00421-016-3366-2
33. Ash GI, Taylor BA, Thompson PD, MacDonald H V., Lamberti L, Chen MH, et al. The antihypertensive effects of aerobic versus isometric handgrip resistance exercise. J Hypertens. 2017;35(2):291–9. https://doi.org/10.1097/HJH.0000000000001176
34. Pagonas N, Vlatsas S, Bauer F, Seibert FS, Zidek W, Babel N, et al. Aerobic versus isometric handgrip exercise in hypertension: A randomized controlled trial. J Hypertens. 2017;35(11):2199–206. https://doi.org/10.1097/HJH. 0000000000001445
35. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. Am J Physiol Endocrinol Metab. 2020;318(5):736–41. https://doi.org/10.1152/ajpendo.00124.2020
36. Cuschieri S, Grech S. COVID-19 and diabetes: The why, the what and the how. J Diabetes Complications. 2020;34(9):107637. https://doi.org/10.1016/j.jdiacomp. 2020.107637

37. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. Cell Metab. 2020;31(6):1068-1077.
https://doi.org/10.1016/j.cmet.2020.04.021
38. Sylow L, Kleinert M, Richter EA, Jensen TE. Exercise-stimulated glucose uptake-regulation and implications for glycaemic control. Nature Reviews Endocrinology. 2017;13(1):133–48.
https://doi.org/10.1038/nrendo. 2016.162
39. Liu Y, Ye W, Chen Q, Zhang Y, Kuo CH, Korivi M. Resistance exercise intensity is correlated with attenuation of HbA1c and insulin in patients with type 2 diabetes: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health. 2019;16(1):140.
http://doi.org/10.3390/ijerph16010140
40. Riddell MC, Gallen IW, Smart CE, Taplin CE, Adolfsson P, Lumb AN, et al. Exercise management in type 1 diabetes: a consensus statement. The Lancet Diabetes and Endocrinology. 2017;5(5):377–90.
https://doi.org/10.1016/S2213-8587(17)30014-1
41. Reddy R, Wittenberg A, Castle JR, El Youssef J, Winters-Stone K, Gillingham M, et al. Effect of Aerobic and Resistance Exercise on Glycemic Control in Adults With Type 1 Diabetes. Can J Diabetes. 2019;43(6):406-14.
https://doi.org/10.1016/j.jcjd.2018.08.193
42. Mitranun W, Deerochanawong C, Tanaka H, Suksom D. Continuous vs interval training on glycemic control and macro- and microvascular reactivity in type 2 diabetic patients. Scand J Med Sci Sport. 2014;24(2):e69-e76.
https://doi.org/10.1111/sms.12112
43. Karstoft K, Winding K, Knudsen SH, Nielsen JS, Thomsen C, Pedersen BK, et al. The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients: A randomized, controlled trial. Diabetes Care. 2013;36(2):228–36.
https://doi.org/10.2337/dc12-0658
44. RezkAllah SS, Takla MK. Effects of different dosages of interval training on glycemic control in people with prediabetes: A randomized controlled trial. Diabetes Spectr. 2019;32(2):125–31.
https://doi.org/10.2337/ds18-0024
45. Tesauro M, Mauriello A, Rovella V, Annicchiarico-Petruzzelli M, Cardillo C, Melino G, et al. Arterial ageing: from endothelial dysfunction to vascular calcification. Journal of Internal Medicine. 2017;281(5):471–82.
https://doi.org/10.1111/joim.12605
46. Frontera WR. Physiologic Changes of the Musculoskeletal System with Aging: A Brief Review. Physical Medicine and Rehabilitation Clinics of North America. 2017;28(4):705–11.
https://doi.org/10.1016/j.pmr.2017.06.004
47. Skloot GS. The Effects of Aging on Lung Structure and Function. Clinics in Geriatric Medicine. 2017;33(4):447–57.
https://doi.org/10.1016/j.cger.2017.06.001
48. Sadighi Akha AA. Aging and the immune system: An overview. Journal of Immunological Methods. 2018;463(1):21–6.
https://doi.org/10.1016/j.jim.2018. 08.005
49. Wilson D, Jackson T, Sapey E, Lord JM. Frailty and sarcopenia: The potential role of an aged immune system. Ageing Research Reviews. 2017;36(1):1–10.
https://doi.org/10.1016/j.arr.2017.01.006
50. Li G, Thabane L, Papaioannou A, Ioannidis G, Levine MAH, Adachi JD. An overview of osteoporosis and frailty in the elderly. BMC Musculoskeletal Disorders. 2017;18(1):46.
https://doi.org/10.1186/s12891-017-1403-x
51. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. The Lancet. 2019;394(10206):1365–75.
https://doi.org/10.1016/S0140-6736(19)31786-6
52. Cesari M, Calvani R, Marzetti E. Frailty in Older Persons. Clinics in Geriatric Medicine. 2017;33(3):293–303.
https://doi.org/10.1016/j.cger.2017.02.002
53. Moccia F, Gerbino A, Lionetti V, Miragoli M, Munaron LM, Pagliaro P, et al. COVID-19-associated cardiovascular morbidity in older adults: a position paper from the Italian Society of Cardiovascular Researches. GeroScience. 2020;42(1):1021-49.
https://doi.org/10.1007/s11357-020-00198-w
54. Nikolich-Zugich J, Knox KS, Tafich Rios C, Natt B, Bhattacharya D, Fain MJ. SARS-CoV-2 and COVID-19 in older adults: what we may expect regarding pathogenesis, immune responses, and outcomes. GeroScience. 2020;42(1):505-14.
https://doi.org/10.1007/s11357-020-00186-0
55. Roman MA, Rossiter HB, Casaburi R. Exercise, ageing and the lung. Eur Respir J. 2016;48(5):1471–86.
http://doi.org/10.1183/13993003.00347-2016
56. Koch LG, Kemi OJ, Qi N, Leng SX, Bijma P, Gilligan LJ, et al. Intrinsic aerobic capacity sets a divide for aging and longevity. Circ Res. 2011;109(10):1162–72.
https://doi.org/10.1161/CIRCRESAHA.111.253807
57. Vigorito C, Giallauria F. Effects of exercise on cardiovascular performance in the elderly.Front. Physiol. 2014;5(1):51.
https://doi.org/10.3389/fphys.2014.00051
58. Vincent KR, Braith RW, Feldman RA, Kallas HE, Lowenthal DT. Improved cardiorespiratory endurance following 6 months of resistance exercise in elderly men and women. Arch Intern Med. 2002;162(6):673–8.
https://doi.org/10.1001/archinte.162.6.673

59. Yoon J-R, Ha G-C, Kang S-J, Ko K-J. Effects of 12-week resistance exercise and interval training on the skeletal muscle area, physical fitness, and mental health in old women. Journal of Exercise Rehabilitation. 2019;15(6):839-47.
https://doi.org/10.12965/jer. 1938644.322
60. Chen HT, Chung YC, Chen YJ, Ho SY, Wu HJ. Effects of Different Types of Exercise on Body Composition, Muscle Strength, and IGF-1 in the Elderly with Sarcopenic Obesity. J Am Geriatr Soc. 2017;65(4):827–32.
http://doi.wiley.com/10.1111/jgs.14722
61. Kim YA, Lee Y, Lee JH, Seo JH. Effects of physical activity on bone mineral density in older adults: Korea National Health and Nutrition Examination Survey, 2008–2011. Arch Osteoporos. 2019;14(1):1–10.
https://doi.org/10.1007/s11657-019-0655-5
62. Beavers KM, Beavers DP, Martin SB, Marsh AP, Lyles MF, Lenchik L, et al. Change in Bone Mineral Density during Weight Loss with Resistance Versus Aerobic Exercise Training in Older Adults. Journals Gerontol - Ser A Biol Sci Med Sci. 2017;72(11):1582–5.
https://doi.org/10.1093/gerona/glx048
63. Roma MFB, Busse AL, Betoni RA, Melo AC de, Kong J, Santarem JM, et al. Effects of resistance training and aerobic exercise in elderly people concerning physical fitness and ability: a prospective clinical trial. Einstein. 2013;11(2):153–7.
http://dx.doi.org/10.1590/S1679-45082013000200003
64. Meng N-H, Li C-I, Liu C-S, Lin C-H, Chang C-K, Chang H-W, et al. Effects of concurrent aerobic and resistance exercise in frail and pre-frail older adults A randomized trial of supervised versus home-based programs. Medicine. 2020;99(29):e21187.
http://dx.doi.org/10.1097/MD. 0000000000021187
65. Minuzzi LG, Rama L, Chupel MU, Rosado F, Dos Santos JV, Simpson R, et al. Effects of lifelong training on senescence and mobilization of T lymphocytes in response to acute exercise. Exerc Immunol Rev. 2018;24(1):72–84.
66. Abd El-Kader SM, Al-Shreef FM. Inflammatory cytokines and immune system modulation by aerobic versus resisted exercise training for elderly. Afr Health Sci. 2018;18(1):120–31.
https://doi.org/10.4314/ahs.v18i1.16
67. Sellami M, Gasmi M, Denham J, Hayes LD, Stratton D, Padulo J, et al. Effects of acute and chronic exercise on immunological parameters in the elderly aged: Can physical activity counteract the effects of aging? Vol. 9, Frontiers in Immunology. 2018;9(1):2187.
https://doi.org/10.3389/fimmu.2018.02187
68. Polastri M, Oldani S, Pisani L, Nava S. Elastic Band Exercises for Patients with Intensive Care Unit-Acquired Weakness: A Case Report. Tanaffos. 2018;17(2):132–7.
69. Medrinal C, Combret Y, Prieur G, Robledo Quesada A, Bonnevie T, Gravier FE, et al. Comparison of exercise intensity during four early rehabilitation techniques in sedated and ventilated patients in ICU: A randomised cross-over trial. Crit Care. 2018;22(1):110.
https://doi.org/10.1186/s13054-018-2030-0
70. Bolton CE, Bevan-Smith EF, Blakey JD, Crowe P, Elkin SL, Garrod R, et al. British Thoracic Society guideline on pulmonary rehabilitation in adults. Thorax. 2013;68(1):ii1-ii30.
http://dx.doi.org/10.1136/thoraxjnl-2013-203808
71. Santos C, Rodrigues F, Santos J, Morais L, Bárbara C. Pulmonary rehabilitation in COPD: Effect of 2 aerobic exercise intensities on subject-centered outcomes—A randomized controlled trial. Respir Care. 2015;60(11):1603–.
https://doi.org/10.4187/respcare.03663
72. Tsai LLY, McNamara RJ, Moddel C, Alison JA, McKenzie DK, McKeough ZJ. Home-based telerehabilitation via real-time videoconferencing improves endurance exercise capacity in patients with COPD: The randomized controlled TeleR Study. Respirology. 2017;22(4):699–707.
https://doi.org/10.1111/resp.12966
73. Bernocchi P, Vitacca M, La Rovere MT, Volterrani M, Galli T, Baratti D, et al. Home-based telerehabilitation in older patients with chronic obstructive pulmonary disease and heart failure: A randomised controlled trial. Age Ageing. 2018;47(1):82–8.
https://doi.org/10.1093/ageing/afx146
74. Chen YW, Wang CY, Lai YH, Liao YC, Wen YK, Chang ST, et al. Home-based cardiac rehabilitation improves quality of life, aerobic capacity, and readmission rates in patients with chronic heart failure. Medicine. 2018;97(4):e9629.
http://doi.org/10.1097/MD.0000000000009629
75. Jiménez-Pavón D, Carbonell-Baeza A, Lavie CJ. Physical exercise as therapy to fight against the mental and physical consequences of COVID-19 quarantine: Special focus in older people. Progress in Cardiovascular Diseases. 2020;63(3):386–8.
https://doi.org/10.1016/j.pcad.2020.03.009
76. Morrey LB, Roberts WO, Wichser L. Exercise-related Mental Health Problems and Solutions during the COVID-19 Pandemic. Curr Sports Med Rep. 2020;19(6):194–95.
https://doi.org/10.1249%2FJSR.0000000000000725
77. Gordon BR, McDowell CP, Hallgren M, Meyer JD, Lyons M, Herring MP. Association of efficacy of resistance exercise training with depressive symptoms meta-analysis and meta-regression: Analysis of randomized clinical trials. JAMA Psychiatry. 2018;75(6):566–76.
https://doi.org/10.1001/jamapsychiatry.2018.0572