COMMENTARY

Sedentariness and physical activity in type 2 diabetes during the COVID-19 pandemic

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In order-to minimize COVID-19 spread, authorities worldwide have ordered stringent lockdown measures.¹ This necessary measure limiting physical activity (PA) results in increasing sedentary time (SED-Time), stress and glycaemic variability. COVID-19 has highlighted the major vulnerability of populations with pre-existing comorbidities.² Type 2 diabetes mellitus (T2DM) is a major comorbidity for COVID-19 progression and adverse endpoints, and well-controlled blood glucose is associated with a significant reduction in the composite of adverse outcomes and death.^{3,4} In a T2DM patients, with or without COVID-19, the goal remain to achieve optimal glycaemic control. To date, it is unclear if good glycaemic control in a T2DM outpatient setting is sufficient to prevent COVID-19, but glycaemic control with a HbA1c <7% and plasma glucose variability maintained between 72 and 144 mg/dL could reduce the risk of infections that might lead to hospitalizations.^{5,6} Such patients setting, if fit, might well benefit from maintained PA, and if sedentary and unfit, would greatly benefit from increased PA and reducing SED-Time.⁷ There are solid evidence that moderate combined aerobic and resistance training programmes are effective in improving daily glucose control, haemoglobin A1c levels and modifiable cardiovascular risk factors in sedentary subjects with T2DM⁸ as well as improving mental health-related quality of life wellbeing.

T2DM patients show an deterioration of the immune system with impaired antiviral activity, inflammatory features of circulating monocytes as well as other immune dysfunctions relevant to T and B cells,⁹⁻¹¹ and chronic low-grade inflammation with altered levels of several pro-inflammatory cytokines, which could predispose them to COVID-19 adverse outcomes.¹² We do not know if PA could enhance immune responses in COVID-19 by attenuating the "cytokine storm syndrome," but we do know that PA in patients with T2DM improves the anti-inflammatory/pro-inflammatory cytokine ratio,¹³ immune defence activity and metabolic health by frequent mobilization and redistribution of effector immune cells (Macrophages, NK cells, CD8⁺ lymphocytes, cytotoxic T cells and immature B cells) and protects the host from several viral

infections.^{10,11} In response to just a single bout of exercise, billions of lymphocytes are licensed to migrate towards peripheral areas, such as the upper respiratory tract, where they can patrol the invasion of pathogens. Virus-specific memory T-cells mobilized with exercise exhibit enhanced proliferation responses to viral antigens such as those derived from CMV, EBV and HSV-1.¹⁰

PA might not prevent us from developing COVID-19 but, as shown from other viral infections, physically active people have less severe symptoms, shorter recovery times, and are less likely to infect others, besides developing better immunity after an anticipated vaccination and minimize future complications, should a second wave of infection occur.¹¹ Epidemiologic and randomized controlled trials have shown that moderate exercise programmes reduce the incidence and duration of upper respiratory tract infections (URTI).¹⁰ Conversely, agonist athletes engaging in marathon races or very intense training are at increased risk of URTI.¹⁴ Thus, strenuous exercise should be carried out individually by fit patients and group activity is not advisable because impaired immune defences and high airflow during the incubation phase and early stages of COVID-19 could facilitate direct penetration of the virus to the lower airways and alveoli, without impacting on the airway's mucosa which are covered by neutralizing antibodies.11

Regular PA guarantees a multitude of beneficial health effects and, especially during this pandemic, its ability to enhance both metabolic health^{13,15} and immune defence^{10,11} could be fundamental. In order to help boost immunity and mitigate the deleterious effects of inactivity and social isolation on our immune and metabolic systems, it is imperative that we strive to maintain recommended levels of PA during this COVID-19 pandemic. There are many creative ways to be physically active that do not require specialized technology and equipment. Keeping active indoors or outdoors through brisk walking, stair climbing, yard or house-work and playing active games can be just as effective. For those who need structured physical exercise, there are numerous free home-based exercise platforms, where virtual trainers offer online instructor-led classes. PA guidelines suggest that to

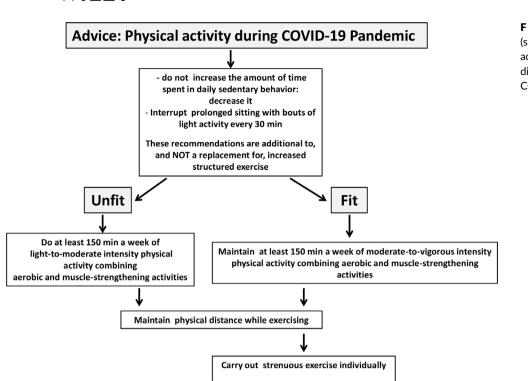


FIGURE 1 Lifestyle (sedentary time and physical activity) suggestions for type 2 diabetes mellitus patients during COVID-19 pandemic

decrease SED-time, adults with T2DM should interrupt prolonged sitting with bouts of light activity every 30 minutes. However, the above recommendations are additional to, and not a replacement for structured exercise that include at least 150 minutes/week of combined aerobic and resistance exercise training (Figure 1).¹⁵

Metabolism and immunity are inextricably interwoven since the metabolic state is a critical determinant of immune function. To strengthen immunometabolic health in T2DM patients, behavioural intervention strategies should be included.¹⁶ Now is the time to adopt every practical measure to reinforce public health both for containing the current pandemic and to be more prepared in case a second wave of infection occurs.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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REFERENCES

- Parmet WE, Sinha MS. Covid-19—the law and limits of quarantine. N Engl J Med. 2020;382(15):e28.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.
- Zhu L, She ZG, Cheng X, 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.e3. https://doi.org/10. 1016/j.cmet.2020.04.021 [Epub 2020 May 1].
- Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev.* 2020;31: e3319. https://doi.org/10.1002/dmrr.3319.

- Yehya A, Carbone S. Managing type 2 diabetes mellitus during COVID-19 pandemic: the bittersweet. *Diabetes Metab Res Rev.* 2020; 3:e3360. https://doi.org/10.1002/dmrr.3360.
- 6. Bornstein SR, Rubino F, Khunti K, et al. Practical recommendations for the management of diabetes in patients with COVID-19. *Lancet Diabetes Endocrinol*. 2020;8:546-550.
- Balducci S, Sacchetti M, Haxhi J, et al. Physical exercise as therapy for type 2 diabetes mellitus. *Diabetes Metab Res Rev.* 2014;30(Suppl. 1):13-23.
- Balducci S, Zanuso S, Nicolucci A, et al. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: a randomized controlled trial: the Italian Diabetes and Exercise Study (IDES). Arch Intern Med. 2010;170 (20):1794-1803.
- 9. Hotamisligil GS. Foundations of immunometabolism and implications for metabolic health and disease. *Immunity*. 2017;47(3):406-420.
- Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. J Sport Health Sci. 2019;8(3):201-217.
- Duggal NA, Niemiro G, Harridge SDR, Simpson RJ, Lord JM. Can physical activity ameliorate immunosenescence and thereby reduce age-related multi-morbidity? *Nat Rev Immunol.* 2019;19:563-572.
- Hu H, Jiang H, Ren H, Hu X, Wang X, Han C. AGEs and chronic subclinical inflammation in diabetes: disorders of immune system. *Diabetes Metab Res Rev.* 2015;31(2):127-137.
- Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovas Dis.* 2010;20:608-617.
- 14. Simpson RJ, Campbell JP, Gleeson M, et al. Can exercise affect immune function to increase susceptibility to infection? *Exerc Immunol Rev.* 2020;26:8-22.
- Colberg SR, Sigal RJ, Yardley JE, et al. Tate DF physical activity/ exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care*. 2016;39(11):2065-2079.
- Balducci S, D'Errico V, Haxhi J, et al. Effect of a behavioral intervention strategy on sustained change in physical activity and sedentary behavior in patients with type 2 diabetes: the IDES_2 randomized clinical trial. JAMA. 2019;321(9):880-890.