Protocol of a systematic review with meta-analysis: The effects of physical exercise/activity on body composition of individuals with cardiometabolic multimorbidity

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Abstract

Multimorbidity can be defined as the combination of 2 or more chronic diseases and affects an increasing number of individuals worldwide. Among the various chronic conditions, cardiometabolic diseases stand out as the main causes of death in the world and their management has been increasingly discussed, from the need for specialized clinics, to the creation of a new medical specialty, to the need for effective interventions. The regular practice of physical activity is an important tool recommended to treat and prevent the worsening of the health status of patients with cardiometabolic diseases. In addition, comprehensive monitoring of cardiometabolic parameters such as body composition is necessary to understand the individual's health status, as well as verify the effectiveness of drug treatments and interventions. It is known that exercise has a beneficial effect on these components, but there is still little evidence exploring its effect on the coexistence of diseases and treatments for populations with cardiometabolic multimorbidity. Thus, the objective of the systematic review is to explore the effects of physical exercise and physical activity on body composition in individuals with cardiometabolic multimorbidity. For this, we will carry out a systematic review with meta-analysis in digital databases (PUBMED, EMBASE, CINAHL, Sportsdiscuss and Prospero).

Keywords: Multiple chronic conditions; Cardiometabolic disease; Physical capacity; Structured exercise; Physical activity recommendation.

Background

Worldwide, more than 60% of the adult population has at least one chronic disease and 20% to 30% are affected by two or more chronic diseases, with cardiometabolic diseases being the most frequent and the main causes of death in the world. People with multiple chronic diseases have a greater chance of hospitalization, longer hospital stay, worse general health status, worse physical and mental function, and lower functional capacity, with an average risk of 50% functional decline with each additional condition[1,2].

Among the non-pharmacological interventions with proven beneficial effects, the practice of physical exercise stands out as an adjuvant treatment and plays an important role in the prevention of cardiometabolic multimorbidity. The practice of a healthier lifestyle, including regular physical activity, was associated with up to 7.6 more years of life for women, improving the general health status of the individual, especially those with multimorbidity. While lower levels of physical activity were associated with increased prevalence of multimorbidity in women aged 16 to 24 years [3,4].

The beneficial effects of physical exercise interventions were demonstrated in the review by Bricca et al, on quality of life outcomes, functional capacity and adverse effects in a population with multimorbidity [5]. However, new approaches to interventions with a multimorbid population are recommended, such as the use of disease patterns to limit the multiple combinations, in addition to interventions aimed at different aspects of the patient, in a multidirectional care [6,7].

Thus, the objective of the review proposed here is to answer the following question: what are the effects of physical exercise and physical activity on body composition, physical capacity and quality of life in individuals with cardiometabolic multimorbidity?

Methods

Eligibility criteria

Studies with the following characteristics will be eligible: **1) Population:** Human, adults (>18y), both sexes and with two or more health conditions, which at least one cardiometabolic (e.g. hypertension, heart failure, coronary artery disease, peripheral artery disease, diabetes, obesity, among others). **2) Intervention:** chronic physical exercise/physical activity of any modality; associated or not with other co-interventions (e.g. diet, behavior change therapy, etc.). **3) Control:** not limited; **4) Outcomes of**

interest; Physical capacity: 6-minute walking test and VO2peak; Body composition: Objectively measured and self-reported body composition (body weight, body mass index, waist circumference); Quality of life; **5) Languages:** English, Portuguese, Italian, French and Spanish**; 6) Study designs:** Intervention studies **7) Publication dates:** The review was restricted to studies published from 2000 onwards.

Search strategy

This study is a spin-off from a scoping review and the studies will be- searched in the following electronic databases: PUBMED, EMBASE, CINAHL, Sportsdiscuss, and Prospero.

Study records

During the screening, eligibility, and data extraction phases, the studies will be evaluated in duplicate by 2 independent reviewers. After checking the reviewers' responses, the disagreements will be resolved by a third reviewer. These studies will be organized in the Mendeley reference manager (https://www.mendeley.com/) and subsequently registered in a spreadsheet for data extraction and organization. If there are studies in which the data are presented only in graphs or figures without clear numerical representation, the data will be extracted by the web-based software WebPlotDigitalizer.

The data extraction will include: 1) the values referring to the outcome of the study (body mass index, body weight, waist circumference); 2) characteristics of the population (sex, exercise training level, average age, and health status), and 3) exercise characteristics (duration, modality, intensity, total volume, associate or not to another intervention).

Risk of bias in individual studies

All included studies will be assessed for risk of bias using the Joanna Briggs Institute Critical Appraisal tool for Randomized Controlled Trials [8]. Bias is assessed as a judgment (Yes, No, Uncertain, n/a) through 13 questions that aim to assess the research design of the study and the validity of its results. In particular, the checklist assesses the randomization of the study, the blinding of participants and treatment providers, the similarities of people in the compared groups and the type of care they received, the existence of pre- and post-intervention measures, the procedures of any follow-up measures, the outcome measure, the reliability of the results, and the adequacy of the statistical analysis.

Methodological quality and risk of bias within included studies will be independently appraised by two reviewers and any disagreements that arose between reviewers will be discussed and resolved by all authors. These data will be presented in the results section in textual and/or graphic form and will help to explore the weaknesses of the studies in the discussion section. In addition, we will describe the conflicts of interest reported by the studies.

Data synthesis and quantitative approaches

The data will be evaluated using the programming language "R" [9] through the supplements "meta" [10] and "metafor" [11]. They will be analyzed based on weighted or standardized mean differences. Kendall's tau and I^2 consistency measures will be presented. The summary meta-analysis values will be presented through a forest plot. If there are sufficient studies, there will be a subgroup analysis dividing them based on the intervention characteristics such as duration (weeks) and volume (total).

Sensitivity analyzes investigated the impact of aspects: exercise modality (aerobic, resistance, combined, yoga, tai chi), type of intervention with exercise (physical exercise or physical activity), type of association in the intervention (exercise only or exercise associated with diet, counseling), gender.

The sensitivity analysis will be done through the search for outliers using the "externally standardized residuals" method, and the search for influential points using the Difference in Fits (DFFITS), Covariance Ratio and Cook's distance methods. Publication bias analyzes will be carried out through a funnel plot and asymmetry hypothesis tests (fail-safe n, Egger and Beggs).

References

[1] R. Palladino, J.T. Lee, M. Ashworth, M. Triassi, C. Millett, Associations between multimorbidity, healthcare utilisation and health status: Evidence from 16 European countries, Age Ageing. 45 (2016) 431–435. https://doi.org/10.1093/ageing/afw044.

[2] C. Reiter-Brennan, O. Dzaye, D. Davis, M. Blaha, R.H. Eckel, Comprehensive Care Models for Cardiometabolic Disease, Curr. Cardiol. Rep. 23 (2021) 1–11. https://doi.org/10.1007/s11886-021-01450-1.

[3] Y. V. Chudasama, K. Khunti, C.L. Gillies, N.N. Dhalwani, M.J. Davies, T. Yates, F. Zaccardi, Healthy lifestyle and life expectancy in people with multimorbidity in the UK Biobank: A longitudinal cohort study, PLoS Med. 17 (2020) 1–18. https://doi.org/10.1371/journal.pmed.1003332.

[4] S. MacMahon, The Academy of Medical Sciences, Multimorbidity: a priority for

global health research, Acad. Med. Sci. (2018). https://acmedsci.ac.uk/file-download/82222577.

[5] Bricca, A., Harris, L. K., Jäger, M., Smith, S. M., Juhl, C. B., & Skou, S. T. (2020). Benefits and harms of exercise therapy in people with multimorbidity: A systematic review and meta-analysis of randomised controlled trials. *Ageing Research Reviews*, *63*, 101166. https://doi.org/10.1016/j.arr.2020.101166

[6] Smith, S. M., Wallace, E., Clyne, B., Boland, F., & Fortin, M. (2021). Interventions for improving outcomes in patients with multimorbidity in primary care and community setting: a systematic review. *Systematic Reviews*, *10*(1). https://doi.org/10.1186/s13643-021-01817-z

[7] Xu, X., Mishra, G. D., & Jones, M. (2017b). Mapping the global research landscape and knowledge gaps on multimorbidity: A bibliometric study. *Journal of Global Health*, *7*(1), 1–11. https://doi.org/10.7189/jogh.07.010414

[8] Aromataris, E., Munn, Z., Campbell, J., & Hopp, L. (2017). JBI Manual for Evidence Synthesis. Chapter 3: Systematic reviews of effectiveness (E. Aromataris & Z. Munn (Eds.)). JBI. https://doi.org/10.46658/JBIMES-20-01

[9] R Core Team. R: a language and environment for statistical computing [Internet]. Vienna R Foundation for Statistical Computing; 2019. Available from: https://www.r-project.org

[10] Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. Evid Based Ment Health. 2019;

[11] Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw. 2010;36:1–48.