Increasing cardiorespiratory fitness as a prognostic intervention: why is it so underrated in clinical practice?

Aumento de la capacidad cardiorrespiratoria como intervención pronóstica: ¿por qué está tan infravalorada en la práctica clínica?

José Kawazoe Lazzoli

Specialist in Sports and Exercise Medicine and Clinical Cardiology. Associate Professor. Biomedical Institute. Fluminense Federal University. Niterói-RJ. Brazil. Head. Cardiology Division. Santa Teresa Hospital. Petrópolis-RJ. Brazil. President. Brazilian Society of Sports and Exercise Medicine (2009/2011). President. Pan-American Confederation of Sports Medicine (2019/2023). Secretary General. International Federation of Sports Medicine (FIMS).

doi: 10.18176/archmeddeporte.00154

Physical activity is widely recognized as a powerful clinical tool, enhancing quality of life and reducing mortality, also contributing to the treatment and/or prevention of several chronic diseases. Seventy years ago, the classical article by Morris *et al.*¹ showed a lower incidence of coronary heart disease in physically active workers, when compared with their inactive counterparts. In the following decades, epidemiological data from longitudinal prospective studies showed a significant reduction on general and cardiovascular mortality, associated with the weekly energy expenditure (volume of exercise)², with exercise intensity providing additional benefit³.

Conversely, physical inactivity is considered by many authors a major public health concern, with huge epidemiological⁴, and economical⁵ consequences, what makes it comparable to a pandemic⁶, with millions of premature deaths each year, and extra billions (whatever currency) spent yearly by the individuals themselves and in the public and private health systems.

In the last two decades, associations were established, between mortality and different measures of sedentary behavior and/or functional capacity. For instance, sitting time and TV/Screen time were associated with a higher mortality in several studies⁷, which was attenuated or eliminated by regular physical activity⁷. In fact, screen time is a major concern in modern society, especially in adolescents, as it is associated with a sedentary lifestyle, with future health implications⁸.

Measurements of functional capacity and mortality

Despite a huge amount of epidemiological data published mainly along 1970s and 1980s, only in this century Exercise capacity (EC) /

Cardiorespiratory Fitness (CRF) began to be recognized as an important marker of longevity. In 2002, Myers *et al.*⁹ studied 6,213 consecutive men referred for treadmill exercise testing for clinical reasons; these subjects were classified into two groups: 3,679 had an abnormal exercise test result or a history of cardiovascular disease; 2,534 had a normal test result and no previous history of cardiovascular disease. After adjustment for age, peak EC in METs was the strongest predictor for the risk of death, both in normal subjects and in those with cardiovascular disease. Each 1-MET increase in EC conferred a 12% improvement in survival.

In the following years, several important studies were published, showing similar results¹⁰⁻¹², showing an unequivocal relation between CRF and mortality. The strong evidence justified a scientific document from the American Heart Association in 2016¹³, stating emphatically that the routine CRF assessment in the clinical setting was as important as a clinical vital sign to be taken: "There is, however, a large body of epidemiological and clinical evidence demonstrating not only that CRF is a potentially stronger predictor of mortality than established risk factors such as smoking, hypertension, high cholesterol, and type 2 diabetes mellitus, but that the addition of CRF to traditional risk factors significantly improves the reclassification of risk for adverse outcomes."

Another Editorial, published eight years ago in Archivos de Medicina del Deporte wondered why physical activity was so undervalued in the reduction of cardiovascular risk, despite of the existing evidence¹⁴.

In fact, CRF improvements are associated with better outcomes in nonfatal cardiovascular events¹⁵, with a 8% reduced risk of developing hypertension for each 1-MET improvement in CRF¹⁶, a reduced risk of developing permanent atrial fibrillation (AF)¹⁷, a better outcome in hypertensive patients with AF¹⁸, a lower risk of developing heart failure¹⁹, a reduced risk of fatal and nonfatal stroke²⁰, a reduced risk of cardiovascular events in subjects with hyperlipidemia²¹, reducing long-term mortality²².

A study by Kokkinos *et al.*²³ showed a reduction of 14% in mortality for each 1-MET increase in a cohort of 750,302 subjects. The benefits occurred independent of gender, ethnic group (White, African-American, Hispanic, Native-American), or age (including septuagenarians and octogenarians). The same author, considering that most studies analyzed only one assessment of CRF, studied the prognostic impact of changes in CRF in two distinct evaluations, separated by at least one year, in 93,606 participants. A decrease of 2,0 METs represented 74% increase in risk for low-fit individuals with cardiovascular disease, and 69% increase in risk for those without CVD. In the whole cohort, inverse and proportionate changes in mortality risk, regardless of previous CRF status were clearly observed²⁴.

As a cardiologist, it is my routine to rigorously observe and pursue clinical goals in my patients, including those with high and very-high cardiovascular risk. It includes LDL-cholesterol goals, HbA1c goals for those who also have diabetes, blood pressure goals, always with the objective of reducing cardiovascular risk, and improving prognosis. Also, recommendations for quitting smoking, reducing body fat percentage, and having better eating habits are often made.

Therefore, I ask you: why aren't we so strong in routinely evaluating CRF in our patients, and in recommending and prescribing physical exercises, a powerful intervention which is known to promote a series of physiological adaptations and clinical improvements, which will ultimately reduce cardiovascular risk? More than seventy years after the pivotal study by Morris, there is certainly enough scientific evidence to justify individualized physical exercise recommendations, not only to all of our patients, but instead to every single person in the world!

Bibliography

- Morris JN, Heady JA, Raffle PAB, Roberts CG, Parks JW. Coronary heart-disease and physical activity of work. *Lancet*. 1953;262:1111-20. DOI: 10.1016/S0140-6736(53)91495-0.
- Paffenbarger Jr RS, Hyde RT, Wing AL. Physical activity, all-cause mortality, and longevity of college alumni. NEng J Med. 1986;314:605-13. DOI: 10.1056/NEJM198603063141003.
- Paffenbarger Jr RS, Lee I-M. Physical activity and fitness for health and longevity. Res Quarterly Exerc Sport. 1996;67:11-28. DOI: 10.1080/02701367.1996.10608850.
- Lee I-M, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet.* 2012;380:219-29. DOI: 10.1016/S0140-6736(12)61031-9.
- Ding D, Lawson KD, Kolbe-Alexander TL, Finkelstein EA, Katzmarzyk PT, van Mechelen W, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *Lancet*. 2016;388(10051):1311-24. DOI: 10.1016/S0140-6736(16)30383-X.
- Kohl 3rd HW, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: global action for public health. *Lancet*. 2012;380:294-305. DOI: 10.1016/S0140-6736(12)60898-8.

- Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell NE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million of men and women. *Lancet.* 2016;388:1302-10. DOI: 10.1016/S0140-6736(16)30370-1.
- Van Sluijs EMF, Ekelund U, Crochemore-Silva I, Guthold R, Ha A, Lubans D, *et al.* Physical activity behavious in adolescence: current evidence and opportunities for intervention. *Lancet.* 2021;398:429:42. DOI: 10.1016/S0140-6736(21)01259-9.
- Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Eng J Med*. 2002;346:793-801. DOI: 10.1056/NEJMoa011858.
- Kokkinos P, Myers J, Kokkinos JP, Pittaras A, Narayan P, Manolis A, et al. Exercise capacity and mortality in black and white men. *Circulation*. 2008;117:614-22. DOI: 10.1161/ CIRCULATIONAHA.107.734764.
- Kokkinos P, Myers J, Faselis C, Panagiotakos DB, Doumas M, Pittaras A, et al. Exercise capacity and mortality in older men: a 20-year follow-up study. *Circulation*. 2010;122: 790-7. DOI: 10.1161/CIRCULATIONAHA.110.938852.
- Laukkanen JA, Zaccardi F, Khan H, Kurl S, Jae SY, Rauramaa R. Long-term change in cardiorespiratory fitness and all-cause mortality: a population-based follow-up study. *Mayo Clin Proc.* 2016;91:1183-8. DOI: 10.1016/j.mayocp.2016.05.014.
- Ross R, Blair SN, Arena R, Church TS, Després JP, Franklin BA, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation*. 2016; 134: e653-99. DOI: 10.1161/CIR.000000000000461.
- 14. Lazzoli JK. Physical activity in the reduction of the cardiovascular risk: too good to be prescribed? *Arch Med Deporte*. 2015;32:205-7.
- Khan H, Jaffar N, Rauramaa R, Kurl S, Savonen K, Laukkanen JA. Cardiorespiratory fitness and nonfatal cardiovascular events: a population-based follow-up study. Am Heart J. 2017;184:55-61. DOI: 10.1016/j.ahj.2016.10.019.
- Cheng C, Zhang D, Chen S, Duan G. The association of cardiorespiratory fitness and the risk of hypertension: a systematic review and a dose-response meta-analysis. J Hum Hypertens. 2022;36:744-52. DOI: 10.1038/s41371-021-00567-8.
- Verdicchio C, Elliott A, Mahajan R, Linz D, Lau D, Sanders P. Greater cardiorespiratory fitness reduces incidence of atrial fibrillation: a meta-analysis. *Eur J Prev Cardiol.* 2021: 28: Suppl 1. DOI: 10.1093/eurjpc/zwab061.200.
- Pittaras A, Grassos C, Faselis C, Tsimploulis A. Atrial fibrillation and mortality risk in hypertensive patients according to cardiorespiratory fitness. J Hypertension. 2023;41 (Suppl 3): e91. DOI: 10.1097/01.hjh.0000939628.80325.bf.
- Kupsky DF, Ahmed AM, Sakr S, Qureshi WT, Brawner CA, Blaha MJ, et al. Cardiorespiratory fitness and incident heart failure: The Henry Ford Exerclse Testing (FIT) Project. Am Heart J. 2017;185:35-42. DOI: 10.1016/j.ahj.2016.12.006.
- Hooker SP, Sui X, Colabianchi N, Vena J, Ladikta J, LaMonte MJ, et al. Cardiorespiratory fitness as a predictor of fatal and nonfatal stroke in asymptomatic women and men. *Stroke*. 2008;39:2950-7. DOI: 10.1161/STROKEAHA.107.495275.
- Hung RK, Al-Mallah MH, Qadi MA, Shaya GE, Blumenthal RS, Nasir K, et al. Cardiorespiratory fitness attenuates risk for major adverse cardiac events in hyperlipidemic men and women independent of statin therapy: The Henry Ford Exercise Testing Project. Am Heart J. 2015;170:390-9. DOI: 10.1016/j.ahj.2015.04.030.
- Mandsager K, Harb S, Cremer P, Phelan D, Nissen SE, Jaber W. Association of cardiorespiratory fitness with long-term mortality among adults undergoing exercise treadmill testing. JAMA Netw Open. 2018;1:e183605. DOI: 10.1001/jamanetworkopen.2018.3605
- Kokkinos P, Faselis C, Samuel IBH, Pittaras A, Doumas M, Murphy R, et al. Cardiorespiratory fitness and mortality risk across the spectra of age, race, and sex. J Am Coll Cardiol. 2022;80:598-69. DOI: 10.1016/j.jacc.2022.05.031.
- Kokkinos P, Faselis C, Samuel IBH, Lavie CJ, Zhang J, Vargas JD, et al. Changes in cardiorespiratory fitness and survival in patients with and without cardiovascular disease. J Am Coll Cardiol. 2023;81:1137-47. DOI: 10.1016/j.jacc.2023.01.027.