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A moderate 1-km treadmill walk predicts mortality in men with mid-range left ventricular dysfunction

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On behalf of my co-authors, I submit for publication on the European Journal of Preventive Cardiology a Letter entitled:

“A moderate 1-km treadmill walk predicts mortality in men with mid-range left ventricular dysfunction”

by:

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I hereby declare that the data presented in this Letter are original and not under consideration or published elsewhere.

Looking forward to hearing from you.

Best regards,

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The manuscript has been modified according to the suggested recommendations.

Best regards,

Simona Mandini, PhD

TITLE**A moderate 1-km treadmill walk predicts mortality in men with mid-range left ventricular dysfunction**

The prevalence of heart failure considerably increased over the last 3 decades because of the aging population and the improved survival rate after acute cardiac events.^{i,ii} Clinical and research programs more frequently are directed to patients with severely impaired functional capacity. Nevertheless, heart failure with mid-range left ventricular dysfunction (HFmrEF) has been recently defined as a distinct clinical entity.ⁱⁱⁱ

Cardiorespiratory fitness (CRF), usually best reflected by peak oxygen consumption (VO_{2peak}), has been shown to be a powerful and independent prognostic marker in patients with heart failure.^{iv-x} CRF has been linked to both cardiovascular and non-cardiovascular outcomes in ambulatory patients with heart failure.ⁱ

VO_{2peak} is strongly related to walking capacity in older adults,^{xi} and among heart failure patients.^{xii} The walking speed maintained during a submaximal 1-km treadmill walk (1k-TWT) has been demonstrated to be a valid and simple tool for VO_{2peak} estimation,^{xiii,xiv} and is inversely related to survival,^{xv-xviii} and hospitalization,^{xviii} in outpatients with cardiovascular disease and preserved left ventricular ejection fraction (LVEF). We examine the association between VO_{2peak} estimated by the 1k-TWT and all-cause mortality in men with HFmrEF.

We studied 209 medically stable male outpatients aged 65 ± 10 years, with LVEF $40\% \pm 5\%$, referred to our exercise-based secondary prevention program. Each patients performed the moderate perceptually-regulated (11-13 on the 6-20 Borg scale) 1k-TWT. Time to walk 1-km, mean and maximal heart rates during the walk, age, height, and weight were entered into the equations for VO_{2peak} estimation.^{xiiii} Based on the VO_{2peak} , the sample was subdivided into tertiles and mortality risks were calculated during a median follow-up of 9.4 year. The local Ethics Committee approved the study protocol, and all subjects gave written informed consent.

Survival decreased in a graded fashion from the highest VO_{2peak} tertile to the lowest tertile ($P < 0.0001$, Figure). During the follow-up period, 23, 11, and 3 all-cause deaths occurred among the lowest, intermediate, and highest VO_{2peak} tertile respectively. Mortality rate was independent from traditional cardiovascular risk factors, including LVEF and clinical history. Compared to the lowest tertile (mean walking speed 2.8 km/h), the full-adjusted mortality risk decreased for the second (mean walking speed 3.8 km/h), and third tertile (mean walking speed 4.6 km/h), with Hazard ratios of 0.64 (95%CI: 0.33-1.20, $P = 0.18$), and 0.26 (95%CI: 0.08-0.80, $P = 0.02$), respectively (P for trend < 0.0001).

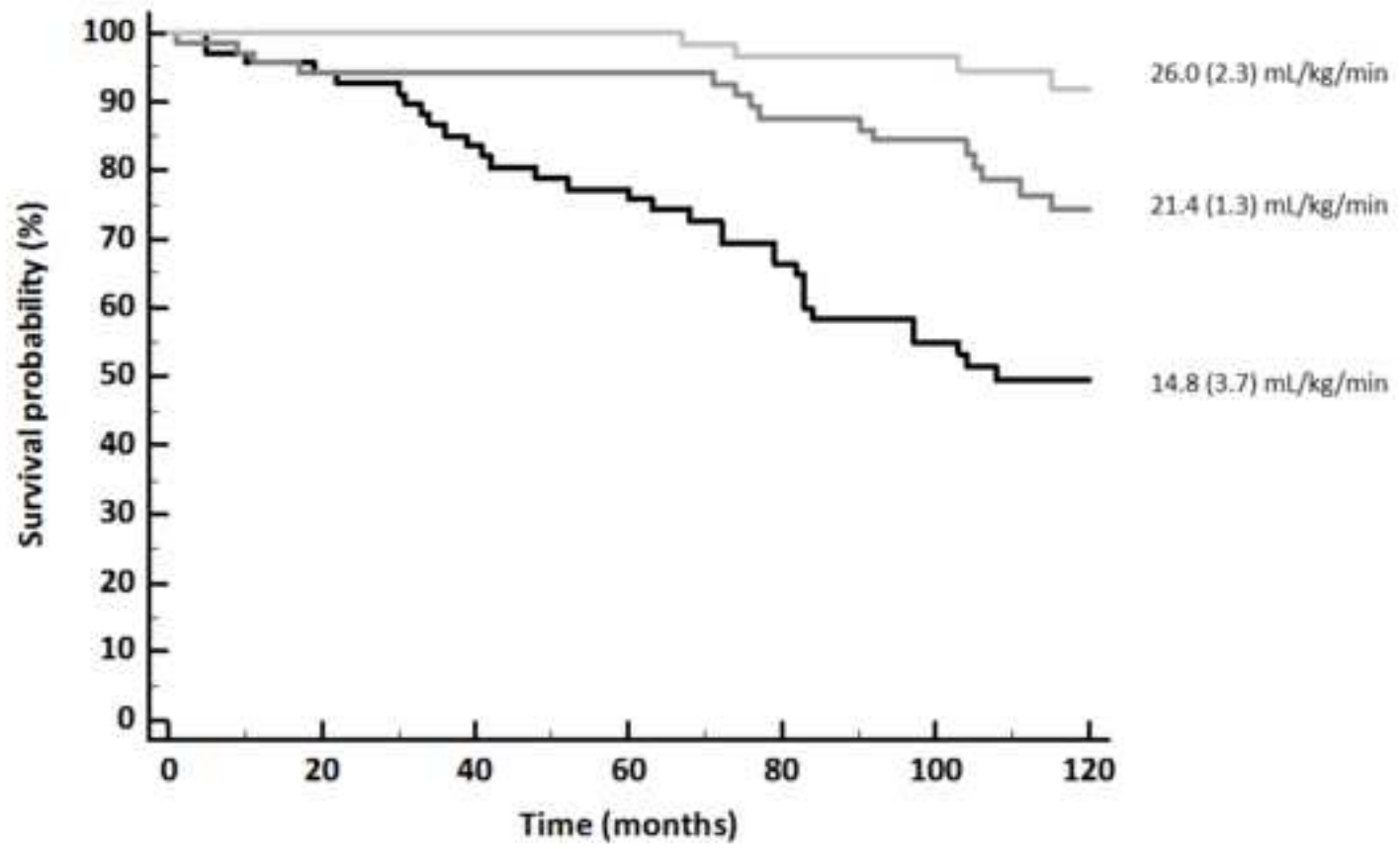
These results are similar to those obtained by other studies in which VO_{2peak} was determined by maximal cardiopulmonary exercise testing.^{xix-xxi} Consistent with previous studies,ⁱ we observed a 24.5% reduction in all-cause mortality associated with each 1-MET increment in VO_{2peak} ($P = 0.04$).

In conclusion, our findings show that VO_2 peak estimated from a simple moderate one-km treadmill-walking test predicts mortality among men with HFmrEF. These results may have practical implications in the context of transitioning from clinically based and supervised training programs to fitness facilities or self-guided exercise programs.

REFERENCES

- I. Ross R, Blair SN, Arena R, 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;CIR.0000000000000461.
- II. Roger VL. Epidemiology of heart failure. *Circ Res* 2013;113:646–659
- III. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;18:891–975
- IV. Corrà U, Mezzani A, Bosimini E, et al. Cardiopulmonary exercise testing and prognosis in chronic heart failure: a prognosticating algorithm for the individual patient. *Chest* 2004;126:942–950
- V. Corrà U, Piepoli MF, Carré F, et al. Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training. *Eur Heart J* 2010;31:1967–1976
- VI. Palau P, Nunez E, Dominguez E, et al. Physical therapy in heart failure with preserved ejection fraction: A systematic review. *Eur J Prev Cardiol* 2014. DOI: 10.1177/2047487314562740
- VII. Fukuta H, Goto T, Wakami K, et al. Effects of drug and exercise intervention on functional capacity and quality of life in heart failure with preserved ejection fraction: A meta-analysis of randomized controlled trials. *Eur J Prev Cardiol* 2014; DOI: 10.1177/2047487314564729
- VIII. Lewinter C, Doherty P, Gale CP, et al. Exercise-based cardiac rehabilitation in patients with heart failure: a meta-analysis of randomized controlled trials between 1999 and 2013. *Eur J Prev Cardiol* 2014; DOI: 10.1177/2047487314559853
- IX. Meijers WC, de Boer RA. Exercise and heart failure: Improve your functional status and your biomarker profile. *Eur J Prev Cardiol* 2017; DOI: 10.1177/2047487317714849
- X. Billebeau G, Vodovar N, Sadoune M, et al. Effects of a cardiac rehabilitation programme on plasma cardiac biomarkers in patients with chronic heart failure. *Eur J Prev Cardiol* 2017; DOI: 10.1177/2047487317705488
- XI. Simonsick EM, Fan E, Fleg JL. Estimating cardiorespiratory fitness in well-functioning older adults: treadmill validation of the long distance corridor walk. *J Am Geriatr Soc* 2006;54:127–132

- XII. Piotrowicz E, Zielinski T, Bodalski R, et al. Home-based telemonitored Nordic walking training is well accepted, safe, and effective and has high adherence among heart failure patients, including those with cardiovascular implantable electronic devices: a randomized controlled study. *Eur J Prev Cardiol* 2014; DOI: 10.1177/2047487314551537
- XIII. Chiaranda G, Myers J, Mazzoni G, et al. Peak oxygen uptake prediction from a moderate, perceptually regulated, 1-km treadmill walk in Male cardiac patients. *J Cardiopulm Rehabil Prev* 2012;32:262–269
- XIV. Grazi G, Chiaranda G, Myers J, et al. Outdoor reproducibility of a 1-km treadmill-walking test to predict peak oxygen consumption in cardiac outpatients. *J Cardiopulm Rehab Prev*, 2017, In press
- XV. Chiaranda G, Bernardi E, Codecà L, et al. Treadmill walking speed and survival prediction in men with cardiovascular disease: a 10-year follow-up study. *BMJ Open* 2013;3:e003446
- XVI. Grazi G, Myers J, Bernardi E, et al. Association between VO₂peak estimated by a 1-km treadmill walk and mortality. A 10-year follow-up study in patients with cardiovascular disease. *Int J Cardiol* 2014;173:248–252
- XVII. Grazi G, Mazzoni G, Myers J, et al. Determining the best percent-predicted equation for estimated VO₂peak by a 1-Km moderate perceptually-regulated treadmill walk to predict mortality in outpatients with cardiovascular disease. *J Sci Med Sport* 2017; in press. DOI: <http://dx.doi.org/10.1016/j.jsams.2017.06.003>
- XVIII. Grazi G, Mazzoni G, Myers J, et al. Improved walking speed is associated with lower hospitalisation rates in patients in an exercise-based secondary prevention programme. *Heart* 2016;102(23):1902-1908
- XIX. Forman DE, Fleg JL, Kitzman DW, et al. 6-min walk test provides prognostic utility comparable to cardiopulmonary exercise testing in ambulatory outpatients with systolic heart failure. *J Am Coll Cardiol* 2012;60(25):2653–2661
- XX. Vanhees L, Fagard R, Thijs L, et al. Prognostic significance of peak exercise capacity in patients with coronary artery disease. *J Am Coll Cardiol* 1994;23(2):358-363
- XXI. Pina IL, Apstein CS, Balady GJ, et al. Exercise and heart failure: a statement from the American Heart Association Committee on exercise, rehabilitation, and prevention. *Circulation* 2003;107:1210-1225



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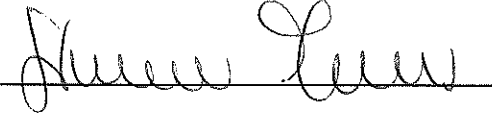
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