UCSF

Title

Exercise Capacity, Heart Failure Risk, and Mortality in Older Adults: The Health ABC Study

Permalink

https://escholarship.org/uc/item/03p7718d

Authors

Georgiopoulou, Vasiliki V
Kalogeropoulos, Andreas P
Chowdhury, Ritam
et al.

Peer reviewed

Exercise Capacity, Heart Failure Risk, and Mortality in Older Adults: The Health ABC Study

Vasiliki V. Georgiopoulou, MD, MPH, PhD[1], **Andreas P. Kalogeropoulos, MD, MPH, PhD**[1], **Ritam Chowdhury, MBBS, MPH, PhD**[2,3], **José Nilo G. Binongo, PhD**[3], **Kirsten Bibbins-Domingo, MD**[4], **Nicolas Rodondi, MD, MAS**[5], **Eleanor M. Simonsick, PhD**[6], **Tamara Harris, MD, MS**[6], **Anne B. Newman, MD, MPH**[7], **Stephen B. Kritchevsky, PhD**[8], and **Javed Butler, MD, MPH, MBA**[9] for the Health ABC Study

[1]Department of Medicine, Division of Cardiology, Emory University, Atlanta, Georgia [2]Department of Biostatistics, Harvard University, Boston, Massachusetts [3]Department of Biostatistics and Bioinformatics, Emory University, Atlanta, Georgia [4]Department of Medicine and Epidemiology and Biostatistics, University of California San Francisco, San Francisco, California [5]Department of General Internal Medicine, University of Bern, Bern, Switzerland [6]Laboratory of Epidemiology, Demography, and Biometry, Intramural Research Program, National Institute on Aging, Baltimore, Maryland [7]Departments of Medicine and Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania [8]Division of Gerontology and Geriatric Medicine, Department of Internal Medicine, Wake Forest University, Winston Salem, North Carolina [9]Department of Medicine, Division of Cardiology, Stony Brook University, Stony Brook, New York

Abstract

Introduction—Data on the association between exercise capacity and risk for heart failure (HF) in older adults are limited.

Methods—This study examined the association of exercise capacity, and its change over time, with 10-year mortality and incident HF in 2,935 participants of the Health, Aging, and Body Composition Study without HF at baseline (age, 73.6 [SD=2.9] years; 52.1% women; 41.4% black; 58.6% white). This cohort was initiated in 1997–1998 and exercise capacity was evaluated with a long distance corridor walk test (LDCW) at baseline and Year 4. Outcomes were collected in 2007–2008 and initial analysis performed in 2014.

Results—Ten-year incident HF for completers (*n*=2,245), non-completers (*n*=331), and those excluded from LDCW for safety reasons (*n*=359) was 11.4%, 19.2%, and 23.0%, respectively. The corresponding 10-year mortality was 27.9%, 41.1%, and 42.4%. In models accounting for competing mortality, the adjusted subhazard ratio for HF was 1.37 (95% CI=1.00, 1.88, *p*=0.049) in non-completers and 1.41 (95% CI=1.06, 1.89, *p*=0.020) in those excluded versus completers.

Address correspondence to: Vasiliki V. Georgiopoulou, MD, MPH, PhD, 1462 Clifton Rd, NE Suite 535A, Atlanta GA 30322. vgeorgi@emory.edu.

Non-completers (adjusted hazard ratio, 1.49; 95% CI=1.21, 1.84; *p*<0.001) and those excluded (hazard ratio, 1.27; 95% CI=1.04, 1.55, *p*=0.016) had elevated mortality. In adjusted models, LDCW performance variables were associated mainly with mortality. Only 20-meter walking speed and resting heart rate retained prognostic value for HF. Longitudinal changes in LDCW did not predict subsequent incident HF or mortality.

Conclusions—Completing an LDCW is strongly associated with lower 10-year mortality and HF risk in older adults. Therefore, walking capacity may serve as an early risk marker.

INTRODUCTION

Exercise capacity is an important indicator of health status and longevity[1] and reflects functional reserves of body systems. Impaired exercise capacity indicates impaired function of body systems and has been associated with increased mortality irrespective of gender, race, or age.[2–8] Low exercise capacity has been associated with risk for hypertension,[9] diabetes mellitus,[10] and cardiovascular events.[11] Responses of the cardiovascular system during exercise strongly predict cardiovascular disease (CVD) and mortality.[12–15] However, data on the association of exercise capacity with risk for heart failure (HF) are limited,[16,17] especially in older adults, who are the population segment with the highest incidence and prevalence of HF.[18]

Tests of varying complexity have been used to evaluate exercise capacity, ranging from distance completed in a predefined time (e.g., the 6-minute walk test) to simultaneous acquisition of several cardiovascular, ventilatory, and gas exchange variables (cardiopulmonary exercise testing). The latter provide pathophysiologic insights that are important for diagnosis,[19] risk assessment,[19] and decision making[19]; however, these tests cannot be widely performed owing to the requirement of special equipment and expertise. Therefore, walking tests have been introduced, allowing for wider implementation of exercise capacity testing; and evaluation of patients who are unable to complete complex protocols because of underlying comorbidities or advanced age. Although the 6-minute walk test is easy to perform, correlates with oxygen consumption,[20,21] and has prognostic value in chronic conditions,[22,23] it has some disadvantages, including a low test ceiling,[24] subject motivation,[25,26] and learning effects.[27] To overcome these drawbacks, the long distance corridor walk test (LDCW) was introduced in the Health, Aging, and Body Composition (Health ABC) study.[28–31] The LDCW helps older individuals approach their maximum capacity,[28] correlates strongly with oxygen consumption,[32] and carries important prognostic information for disability, CVD, and all-cause mortality.[7] However, the value of LDCW and, importantly, the value of changes in exercise performance over time for HF risk prediction, have not been evaluated.

In this study, the association of LDCW parameters, and their change over time, with long-term risk for all-cause mortality and incident HF, using 10-year follow-up data from the Health ABC study was examined. In secondary analyses, the association of LDCW parameters with outcomes of interest in sex and race subgroups and in participants with and without CVD at baseline was examined.

METHODS

Study Population

The Health ABC study is a community-based study of 3,075 well-functioning individuals aged 70–79 years at inception (April 1997–June 1998).[7,33] Exclusion criteria included difficulty walking a quarter of a mile, climbing stairs or performing basic activities of daily living, obvious cognitive impairment, inability to communicate, anticipated move within 3 years, or participation in a trial involving lifestyle intervention.[33] The IRBs at both sites and the coordinating center approved the study. At baseline and at Year 4, participants were asked to undergo a LDCW test to evaluate their exercise capacity. This analysis included data on 2,935 participants; 140 participants with either prevalent HF or inconclusive or missing data on HF at baseline were excluded. For outcomes, adjudicated 10-year follow-up data, collected in 2007–2008, were used. Initial analysis of these data was performed in 2014.

Measures

The LDCW was used as an objective measure of participants' exercise capacity and as a verification of their self-reported ability to walk a quarter of a mile. Participants were divided into:

1. completers, those who completed the LDCW test;

2. non-completers, those who started but did not complete both phases of the LDCW test; and

3. those excluded from LDCW for safety reasons because of electrocardiogram abnormalities, elevated blood pressure (200/110 mmHg), resting heart rate >135 beats/minute or <40 beats/minute, recent exacerbation of chest pain, shortness of breath, or a recent cardiac event or procedure.

The LCDW test has two stages.[34] Stage 1 is a 2-minute warm-up. The walking speed to cover the first 20 meters of the warm-up was recorded and the steps needed to complete 20 meters were also measured. Stage 2 is a 400-meter walk in a hallway, where participants are instructed to walk as quickly as they can at a steady pace. Standardized encouragement was given. Heart rate was monitored continuously. Participants could stop the test because of fatigue or symptoms. The staff stopped the test if persistent tachycardia (>135 beats/minute) occurred. The distance covered in the first 2 minutes and the time needed for completion of the 400-meter walk were recorded. Blood pressure and heart rate response, including heart rate recovery (change from the end of test until 2 minutes after) were also recorded.

Race was self-defined by participants. Smoking was defined as current, past (100 lifetime cigarettes), or never. Leg length was calculated as the average standing height measurement minus the hip-to-head measurement. Physical activity was determined using a standardized questionnaire designed specifically for the Health ABC study.[35,36]

Baseline CVD status (including HF) was based on ICD 9-CM codes as reported by Medicare Services for years 1995–1998, self-reported history, and medications. Following

the definitions used in previous Health ABC work,[7,37] prevalent CVD was defined as prevalent:

1. coronary heart disease;

2. cerebrovascular disease; or

3. peripheral vascular disease.

Incident CVD was defined as:

1. incident coronary heart disease;

2. incident cerebrovascular disease;

3. incident peripheral arterial disease; or

4. death due to cardiovascular causes.

Definitions of diabetes, hypertension, depression, and pulmonary disease used in previous studies were followed.[33,38] Left ventricular hypertrophy was determined from electrocardiography.[38]

Participants were surveyed every 6 months for interim events. Local adjudicators reviewed medical records for overnight hospitalizations. Using algorithms mirroring those of the Cardiovascular Health Study, a panel of clinicians verified diagnoses and causes of death based on interview, review of hospital records, and death certificates. All first admissions with an overnight stay confirmed as related to HF, using the criteria of the Cardiovascular Health Study, were considered as incident HF events.[39] The criteria required HF diagnosis by a physician and treatment for HF.[40] Briefly, HF was confirmed if there was documentation of symptoms and signs, supporting imaging findings, or medical therapy for HF, including at least a diuretic and a vasodilator or digitalis. Incident CVD events were identified and adjudicated using the standard Health ABC surveillance and adjudication process described above. The Health ABC Diagnosis and Disease Ascertainment Committee reviewed all deaths.

Statistical Analysis

Differences in baseline characteristics across LDCW completion categories were examined with the Kruskal–Wallis and chi-square tests for continuous and categorical variables, respectively. The association of LDCW performance and cardiovascular response parameters with mortality was examined with Cox proportional hazards models. For incident HF, Fine and Gray models were used to account for competing mortality.[41] The analyses for changes from Year 1 to Year 4 and subsequent mortality and incident HF were repeated. A simulation approach (PROC PHREG/ASSESS) was used to identify potential nonlinear associations of LDCW parameters with the events of interest. The proportional hazards assumption was evaluated using the Schoenfeld residuals for Cox models and interaction terms with time for Fine and Gray models.

Multivariable analyses included:

1.   risk factors previously associated with mortality and incident HF in Health ABC;

2.   factors that could affect exercise capacity; and

3.   additional baseline characteristics associated with exercise capacity.

All tests of hypotheses were two-sided at the α=0.05 level. Analyses were performed with Stata, version 13.1 and SAS, version 9.4.

RESULTS

The mean age of participants (N=2,935) was 73.6 (SD=2.9) years, 52.1% were women, and 41.4% were black. Table 1 summarizes the baseline characteristics according to LDCW test completion category. Men, whites, and participants with greater reported physical activity were more likely to complete the test. Those with hypertension, diabetes, and CVD were more likely to stop. Lower resting heart rate and systolic blood pressure, and absence of electrocardiographic abnormalities were associated with test completion. Performance data and cardiovascular responses of test completers are summarized in Table 2.

After 10 years of follow-up, 620/2,245 test completers died as compared with 135/331 test non-completers and 151/359 participants who were excluded. The corresponding Kaplan–Meier estimates for 10-year mortality were 27.9% (95% CI=26.1%, 29.8%), 41.1% (95% CI=36.0%, 46.7%), and 42.4% (95% CI=37.4%, 47.8%) (log-rank chi-square=52.2, p<0.001, Figure 1A). Among completers, 253 (11.3%) developed HF as compared with 63 (19.0%) among non-completers and 82 (22.8%) among those who were excluded. The 10-year cumulative HF incidence was 11.4% (95% CI=10.2%, 12.7%), 19.2% (95% CI=15.8%, 23.3%), and 23.0% (95% CI=18.9%, 27.9%), respectively (Figure 1B).

In unadjusted models, the mortality hazard ratio (HR) was 1.69 (95% CI=1.41, 2.02, p<0.001) for those excluded and 1.64 (95% CI=1.36, 1.98, p<0.001) for non-completers, with completers as reference. In models adjusting for the covariates described in Table 1, the increased mortality risk persisted; the adjusted HR was 1.27 (95% CI=1.04, 1.55, p=0.016) for those excluded and 1.49 (95% CI=1.21, 1.84, p<0.001) for non-completers.

In models accounting for competing mortality, the subhazard ratio (sHR) for HF was 2.17 (95% CI=1.69, 2.79, p<0.001) for those excluded and 1.77 (95% CI=1.34, 2.33, p<0.001) for non-completers, with completers as reference. In competing-risks models adjusting for the covariates described in Table 1, sHR for HF was 1.41 (95% CI=1.06, 1.89, p=0.020) for those excluded and 1.37 (95% CI=1.00, 1.88, p=0.049) for non-completers.

Among completers (n=2,245), all exercise performance variables were strongly associated with 10-year mortality in unadjusted and adjusted models, with the walking speed to cover 400 meters being the strongest predictor (Table 3). Specifically, mortality risk was lower by approximately 78% for every meter/second-faster walking speed. Among cardiovascular responses, univariate predictors of mortality were (Table 3):

1.   heart rate change from rest to 2 minutes and 400 meters;

2. heart rate recovery; and

3. change in diastolic blood pressure.

However, these associations were attenuated in adjusted models; only the change in diastolic blood pressure retained a trend toward statistical significance with risk increasing in parallel with diastolic blood pressure increases.

All exercise performance variables, baseline systolic blood pressure and heart rate, and change in heart rate from rest to 2 minutes were associated with increased risk of HF in univariate models (Table 3). Higher walking speed to cover the first 20 meters of the warm-up phase, the 400 meters of the second phase, and larger distance covered during the warm-up phase were associated with lower HF risk. Higher baseline systolic blood pressure and heart rate were associated with higher HF risk. However, in adjusted models, only the walking speed to cover the first 20 meters of the warm-up phase and the baseline heart rate retained statistical significance (Table 3). Specifically, for every meter/second-faster walking speed, the HF risk was lower by approximately 55%.

Subgroup Analyses

Analyses for significant interactions between LDCW responses and sex, race, and baseline CVD for mortality and incident HF risk were performed. Systolic blood pressure response to LDCW was differentially associated with 10-year mortality in men versus women; SBP at the end of 400-meter walk had an unadjusted HR of 0.996 per mmHg (95% CI=0.992, 1.000, p=0.073) in men versus 1.007 (95% CI=1.002, 1.012, p=0.007) in women (p=0.001 for interaction). This interaction persisted in adjusted models (p=0.018), although the individual HRs were not statistically significant: 1.000 per mmHg (95% CI=0.994, 1.005, p=0.86) in men versus 1.003 (95% CI=0.996, 1.009, p=0.45) in women. No other significant interactions were detected.

Both the absolute values of Year 4 LDCW parameters and the corresponding changes from baseline as predictors for the remaining 6-year horizon were evaluated. Among the 2,245 participants who completed the test at baseline, 1,418 (63.2%) participants without interim HF completed the Year 4 LCDW test. Although overall speed to complete 400 meters decreased by 0.03 (SD=0.12) meters/second (p<0.001) to 1.25 (SD=0.21) meters/second, the distance covered during the first 2 minutes increased by 1.8 (SD=21.6) meters (p=0.001) to 162 (SD=27) meters.

The association of LDCW performance with mortality among Year 4 completers is presented in Appendix Table 1. In unadjusted models, both absolute values of distance covered by 2 minutes and speed to walk 400 meters and their changes from Year 1 to Year 4 were associated with mortality. However, in adjusted analysis, only absolute values at Year 4 retained statistical significance (Appendix Table 1). Neither absolute Year 4 LDCW performance variables nor their changes from Year 1 demonstrated significant associations with incident HF (data not shown).

DISCUSSION

In this study, an association between exercise capacity, assessed by the LDCW test, and incident HF among older adults participating in the Health ABC study was observed. Also, the ability to complete the LDCW test was a strong predictor of both 10-year incident HF and 10-year mortality. A strong association was also observed between baseline exercise capacity and long-term mortality among these healthy older individuals. All measures of LDCW performance were predictors of mortality, the strongest being the speed to cover 400 meters. Among the measures of LDCW performance, walking speed over the first 20 meters of the warm-up phase was the stronger predictor of incident HF. Another important finding of this study was that changes in exercise capacity from Year 1 to 4 were not associated with subsequent mortality, although the absolute performance at Year 4 was strongly associated with death over the next 6 years. Year 4 LDCW performance did not predict subsequent incident HF, perhaps reflecting selection bias since only relatively fit participants were still alive and able to take the Year 4 test. This is the first study reporting on the association of exercise capacity and its longitudinal changes with mortality and incident HF in a well-functioning older population.

Most data on the association between exercise capacity and mortality come from studies using laboratory tests. Limited data have linked performance in walking tests with mortality in healthy individuals.[7,8] The findings of this study on mortality are in accordance with the findings of a study by Stanaway et al.,[42] where walking speed of 0.82 meters/second was associated with high mortality in older healthy individuals. The current study expands the previous findings on mortality[7] with a longer-term follow-up (10 years), data on HF risk, and competing risks estimates for HF to account for the high rates of 10-year mortality in this older population. Although walking tests are often used in populations with chronic health conditions, these inexpensive tests can also be useful in healthy individuals and especially older adults, who may have difficulty undergoing a laboratory exercise test. This is further supported by the association of LDCW performance with clinical or subclinical disease in older adults.[34]

The observed weak association between exercise performance and incident HF are not aligned with recent data on the prognostic value of exercise performance for incident HF in middle-aged adults.[16,17] In these studies, the evaluation of exercise capacity was done by maximal exercise tests. There are important differences in the granularity of information gained from field and laboratory tests. For example, heart rate or blood pressure increases are smaller during field tests.[43] However, field tests represent activities of daily living better than laboratory tests, thus offering significant information on health status.[44] The discrepancy of the prognostic value of laboratory versus field tests cannot be attributed solely to the different exercise testing methods. A possible explanation could be that Health ABC Study participants were well-functioning individuals by design. Also, considering that mortality is higher in this age group than in middle-aged adults, the association of exercise capacity with HF may be attenuated because of competing mortality. Finally, the authors adjusted for a large array of risk factors associated with incident HF. These risk factors have also been associated with exercise capacity, and therefore confounding may be an additional explanation for the attenuated association of exercise capacity with HF risk in this study.

Several possible mechanisms could link exercise capacity to risk for HF. Physical inactivity leads to elevated levels of blood pressure and serum lipids, insulin resistance, and obesity, all of which predispose to the development of HF.[10,45] On the other hand, regular physical activity may increase the capacity of endothelial cells to evoke vasodilatation in the early stages of atherosclerosis, thus retarding its progression and preventing CVD development.[46,47] Physical activity also protects against the development of CVD by favorably affecting risk factors[48–54] and may help improve cardiac output, left ventricular function and oxygen utilization, and the formation of collateral vessels.[46,55,56] Physical activity seems to regulate cardiac autonomic function and vagal control of heart rate, therefore reducing risk of ventricular arrhythmias and subsequent risk of HF.[57] This is supported in this study also, as resting heart rate remained an independent risk factor for HF development.

In this population, there was a small decline in exercise performance over time, with a decrease of average walking speed beyond 400 meters. Although exercise capacity at Year 4 was strongly associated with mortality, it was not associated with HF, a finding that supports the assumption that mortality may precede HF development in older adults and especially in those of higher risk, inducing selection bias over time.

Limitations

This study has several limitations. Although participants were well characterized, thus providing sufficient information to control for confounders and arrive at conclusions as valid as possible, unobserved confounding cannot be excluded. Selection bias toward healthier older adults is inherent in this study. Thus, these findings apply only to well-functioning older adults. Careful interpretation is required for other older adult groups. Considering the 10-year horizon, the possibility of regression dilution cannot be excluded. Although there is some potential for bias because of loss to follow-up, the retention rate in the study was very high, limiting this bias. Older age is associated with higher mortality rates, which can affect estimates for competing outcomes. However, in this analysis, the authors did account for death as a competing event factor in incident HF analyses to avoid inflation of HF risk estimates.

CONCLUSIONS

This study highlights the strong prognostic value of exercise capacity as evaluated by a field test (LDCW) with mortality and risk for HF in well-functioning older adults, despite the association of exercise capacity with HF risk being weaker. In addition, longitudinal changes in exercise capacity were not associated with mortality or HF risk. However, older adults have a higher competing risk for mortality before developing HF. Therefore, interventional studies are needed to evaluate whether improved exercise capacity may result in improved survival, less HF, and better quality of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

1. Gulati M, Black HR, Shaw LJ, et al. The prognostic value of a nomogram for exercise capacity in women. N Engl J Med. 2005; 353(5):468–475. http://dx.doi.org/10.1056/NEJMoa044154. [PubMed: 16079370]

2. Blair SN, Kampert JB, Kohl HW 3rd, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA. 1996; 276(3):205–210. http://dx.doi.org/10.1001/jama.1996.03540030039029. [PubMed: 8667564]

3. Blair SN, Kohl HW 3rd, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA. 1989; 262(17): 2395–2401. http://dx.doi.org/10.1001/jama.1989.03430170057028. [PubMed: 2795824]

4. Kokkinos P, Myers J, Kokkinos JP, et al. Exercise capacity and mortality in black and white men. Circulation. 2008; 117(5):614–622. http://dx.doi.org/10.1161/CIRCULATIONAHA.107.734764. [PubMed: 18212278]

5. Sandvik L, Erikssen J, Thaulow E, Erikssen G, Mundal R, Rodahl K. Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. N Engl J Med. 1993; 328(8):533–537. http://dx.doi.org/10.1056/NEJM199302253280803. [PubMed: 8426620]

6. Sui X, Laditka JN, Hardin JW, Blair SN. Estimated functional capacity predicts mortality in older adults. J Am Geriatr Soc. 2007; 55(12):1940–1947. http://dx.doi.org/10.1111/j.1532-5415.2007.01455.x. [PubMed: 17979958]

7. Newman AB, Simonsick EM, Naydeck BL, et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA. 2006; 295(17):2018–2026. http://dx.doi.org/10.1001/jama.295.17.2018. [PubMed: 16670410]

8. Yazdanyar A, Aziz MM, Enright PL, et al. Association Between 6-Minute Walk Test and All-Cause Mortality, Coronary Heart Disease-Specific Mortality, and Incident Coronary Heart Disease. J Aging Health. 2014; 26(4):583–599. http://dx.doi.org/10.1177/0898264314525665. [PubMed: 24695552]

9. Blair SN, Goodyear NN, Gibbons LW, Cooper KH. Physical fitness and incidence of hypertension in healthy normotensive men and women. JAMA. 1984; 252(4):487–490. http://dx.doi.org/10.1001/jama.1984.03350040017014. [PubMed: 6737638]

10. Wei M, Gibbons LW, Mitchell TL, Kampert JB, Lee CD, Blair SN. The association between cardiorespiratory fitness and impaired fasting glucose and type 2 diabetes mellitus in men. Ann Intern Med. 1999; 130(2):89–96. http://dx.doi.org/10.7326/0003-4819-130-2-199901190-00002. [PubMed: 10068380]

11. Peterson PN, Magid DJ, Ross C, et al. Association of exercise capacity on treadmill with future cardiac events in patients referred for exercise testing. Arch Intern Med. 2008; 168(2):174–179. http://dx.doi.org/10.1001/archinternmed.2007.68. [PubMed: 18227364]

12. Cole CR, Foody JM, Blackstone EH, Lauer MS. Heart rate recovery after submaximal exercise testing as a predictor of mortality in a cardiovascularly healthy cohort. Ann Intern Med. 2000;

132(7):552–555. http://dx.doi.org/10.7326/0003-4819-132-7-200004040-00007. [PubMed: 10744592]

13. Lauer MS, Okin PM, Larson MG, Evans JC, Levy D. Impaired heart rate response to graded exercise. Prognostic implications of chronotropic incompetence in the Framingham Heart Study. Circulation. 1996; 93(8):1520–1526. http://dx.doi.org/10.1161/01.CIR.93.8.1520. [PubMed: 8608620]

14. Jouven X, Empana JP, Schwartz PJ, Desnos M, Courbon D, Ducimetiere P. Heart-rate profile during exercise as a predictor of sudden death. N Engl J Med. 2005; 352(19):1951–1958. http://dx.doi.org/10.1056/NEJMoa043012. [PubMed: 15888695]

15. McHam SA, Marwick TH, Pashkow FJ, Lauer MS. Delayed systolic blood pressure recovery after graded exercise: an independent correlate of angiographic coronary disease. J Am Coll Cardiol. 1999; 34(3):754–759. http://dx.doi.org/10.1016/S0735-1097(99)00269-7. [PubMed: 10483957]

16. Farrell SW, Finley CE, Radford NB, Haskell WL. Cardiorespiratory fitness, body mass index, and heart failure mortality in men: Cooper Center Longitudinal Study. Circ Heart Fail. 2013; 6(5):898–905. http://dx.doi.org/10.1161/CIRCHEARTFAILURE.112.000088. [PubMed: 23873472]

17. Khan H, Kunutsor S, Rauramaa R, et al. Cardiorespiratory fitness and risk of heart failure: a population-based follow-up study. Eur J Heart Fail. 2014; 16(2):180–188. http://dx.doi.org/10.1111/ejhf.37. [PubMed: 24464981]

18. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010; 121(7):e46–e215. http://dx.doi.org/10.1161/CIRCULATIONAHA.109.192667. [PubMed: 20019324]

19. Sue DY, Wasserman K. Impact of integrative cardiopulmonary exercise testing on clinical decision making. Chest. 1991; 99(4):981–992. http://dx.doi.org/10.1378/chest.99.4.981. [PubMed: 2009806]

20. Peeters P, Mets T. The 6-minute walk as an appropriate exercise test in elderly patients with chronic heart failure. J Gerontol A Biol Sci Med Sci. 1996; 51(4):M147–151. http://dx.doi.org/10.1093/gerona/51A.4.M147. [PubMed: 8680996]

21. Cahalin L, Pappagianopoulos P, Prevost S, Wain J, Ginns L. The relationship of the 6-min walk test to maximal oxygen consumption in transplant candidates with end-stage lung disease. Chest. 1995; 108(2):452–459. http://dx.doi.org/10.1378/chest.108.2.452. [PubMed: 7634883]

22. Bittner V, Weiner DH, Yusuf S, et al. Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. SOLVD Investigators. JAMA. 1993; 270(14):1702–1707. http://dx.doi.org/10.1001/jama.1993.03510140062030. [PubMed: 8411500]

23. Casanova C, Cote C, Marin JM, et al. Distance and oxygen desaturation during the 6-min walk test as predictors of long-term mortality in patients with COPD. Chest. 2008; 134(4):746–752. http://dx.doi.org/10.1378/chest.08-0520. [PubMed: 18625667]

24. Frost AE, Langleben D, Oudiz R, et al. The 6-min walk test (6MW) as an efficacy endpoint in pulmonary arterial hypertension clinical trials: demonstration of a ceiling effect. Vascul Pharmacol. 2005; 43(1):36–39. http://dx.doi.org/10.1016/j.vph.2005.03.003. [PubMed: 15890561]

25. Guyatt GH, Pugsley SO, Sullivan MJ, et al. Effect of encouragement on walking test performance. Thorax. 1984; 39(11):818–822. http://dx.doi.org/10.1136/thx.39.11.818. [PubMed: 6505988]

26. Clark AL, Poole-Wilson PA, Coats AJ. Effects of motivation of the patient on indices of exercise capacity in chronic heart failure. Br Heart J. 1994; 71(2):162–165. http://dx.doi.org/10.1136/hrt.71.2.162. [PubMed: 8130025]

27. Wu G, Sanderson B, Bittner V. The 6-minute walk test: how important is the learning effect? Am Heart J. 2003; 146(1):129–133. http://dx.doi.org/10.1016/S0002-8703(03)00119-4. [PubMed: 12851620]

28. Simonsick EM, Montgomery PS, Newman AB, Bauer DC, Harris T. Measuring fitness in healthy older adults: the Health ABC Long Distance Corridor Walk. J Am Geriatr Soc. 2001; 49(11):1544–1548. http://dx.doi.org/10.1046/j.1532-5415.2001.4911247.x. [PubMed: 11890597]

29. Simonsick EM, Newman AB, Nevitt MC, et al. Measuring higher level physical function in well-functioning older adults: expanding familiar approaches in the Health ABC study. J Gerontol A Biol Sci Med Sci. 2001; 56(10):M644–649. http://dx.doi.org/10.1093/gerona/56.10.M644. [PubMed: 11584038]

30. Simonsick EM, Newman AB, Visser M, et al. Mobility limitation in self-described well-functioning older adults: importance of endurance walk testing. J Gerontol A Biol Sci Med Sci. 2008; 63(8):841–847. http://dx.doi.org/10.1093/gerona/63.8.841. [PubMed: 18772472]

31. Klepin HD, Geiger AM, Tooze JA, et al. Physical performance and subsequent disability and survival in older adults with malignancy: results from the health, aging and body composition study. J Am Geriatr Soc. 2010; 58(1):76–82. http://dx.doi.org/10.1111/j.1532-5415.2009.02620.x. [PubMed: 20122042]

32. 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(1):127–132. http://dx.doi.org/10.1111/j.1532-5415.2005.00530.x. [PubMed: 16420209]

33. Georgiopoulou VV, Kalogeropoulos AP, Psaty BM, et al. Lung function and risk for heart failure among older adults: the Health ABC Study. Am J Med. 2011; 124(4):334–341. http://dx.doi.org/10.1016/j.amjmed.2010.12.006. [PubMed: 21435424]

34. Newman AB, Haggerty CL, Kritchevsky SB, Nevitt MC, Simonsick EM. Health ABCCRG. Walking performance and cardiovascular response: associations with age and morbidity--the Health, Aging and Body Composition Study. J Gerontol A Biol Sci Med Sci. 2003; 58(8):715–720. http://dx.doi.org/10.1093/gerona/58.8.M715. [PubMed: 12902529]

35. Taylor HL, Jacobs DR Jr, Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. J Chronic Dis. 1978; 31(12):741–755. http://dx.doi.org/10.1016/0021-9681(78)90058-9. [PubMed: 748370]

36. Brach JS, Simonsick EM, Kritchevsky S, Yaffe K, Newman AB. The association between physical function and lifestyle activity and exercise in the health, aging and body composition study. J Am Geriatr Soc. 2004; 52(4):502–509. http://dx.doi.org/10.1111/j.1532-5415.2004.52154.x. [PubMed: 15066063]

37. Cesari M, Penninx BW, Newman AB, et al. Inflammatory markers and cardiovascular disease (The Health, Aging and Body Composition [Health ABC] Study). Am J Cardiol. 2003; 92(5):522–528. http://dx.doi.org/10.1016/S0002-9149(03)00718-5. [PubMed: 12943870]

38. Butler J, Kalogeropoulos A, Georgiopoulou V, et al. Incident heart failure prediction in the elderly: the health ABC heart failure score. Circ Heart Fail. 2008; 1(2):125–133. http://dx.doi.org/10.1161/CIRCHEARTFAILURE.108.768457. [PubMed: 19777072]

39. Fried LP, Borhani NO, Enright P, et al. The Cardiovascular Health Study: design and rationale. Ann Epidemiol. 1991; 1(3):263–276. http://dx.doi.org/10.1016/1047-2797(91)90005-W. [PubMed: 1669507]

40. Rodondi N, Newman AB, Vittinghoff E, et al. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Arch Intern Med. 2005; 165(21):2460–2466. http://dx.doi.org/10.1001/archinte.165.21.2460. [PubMed: 16314541]

41. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. J Am Stat Assoc. 1999; 94(446):496–509. http://dx.doi.org/10.1080/01621459.1999.10474144.

42. Stanaway FF, Gnjidic D, Blyth FM, et al. How fast does the Grim Reaper walk? Receiver operating characteristics curve analysis in healthy men aged 70 and over. BMJ. 2011; 343:d7679. http://dx.doi.org/10.1136/bmj.d7679. [PubMed: 22174324]

43. Ingle L, Rigby AS, Sloan R, et al. Development of a composite model derived from cardiopulmonary exercise tests to predict mortality risk in patients with mild-to-moderate heart failure. Heart. 2014; 100(10):781–786. http://dx.doi.org/10.1136/heartjnl-2013-304614. [PubMed: 24567314]

44. Georgiopoulou V. Laboratory versus field walking tests in moderate COPD: value in simplicity? Respirology. 2012; 17(2):197–198. http://dx.doi.org/10.1111/j.1440-1843.2011.02119.x. [PubMed: 22221901]

45. Rankinen T, Church TS, Rice T, Bouchard C, Blair SN. Cardiorespiratory fitness, BMI, and risk of hypertension: the HYPGENE study. Med Sci Sports Exerc. 2007; 39(10):1687–1692. http://dx.doi.org/10.1249/mss.0b013e31812e527f. [PubMed: 17909393]

46. Hambrecht R, Wolf A, Gielen S, et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. N Engl J Med. 2000; 342(7):454–460. http://dx.doi.org/10.1056/NEJM200002173420702. [PubMed: 10675425]

47. Niebauer J, Hambrecht R, Velich T, et al. Attenuated progression of coronary artery disease after 6 years of multifactorial risk intervention: role of physical exercise. Circulation. 1997; 96(8):2534–2541. http://dx.doi.org/10.1161/01.CIR.96.8.2534. [PubMed: 9355890]

48. Tran ZV, Weltman A, Glass GV, Mood DP. The effects of exercise on blood lipids and lipoproteins: a meta-analysis of studies. Med Sci Sports Exerc. 1983; 15(5):393–402. http://dx.doi.org/10.1249/00005768-198315050-00009. [PubMed: 6645868]

49. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. N Engl J Med. 2002; 347(19):1483–1492. http://dx.doi.org/10.1056/NEJMoa020194. [PubMed: 12421890]

50. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001; 344(18):1343–1350. http://dx.doi.org/10.1056/NEJM200105033441801. [PubMed: 11333990]

51. Stewart KJ. Exercise training and the cardiovascular consequences of type 2 diabetes and hypertension: plausible mechanisms for improving cardiovascular health. JAMA. 2002; 288(13):1622–1631. http://dx.doi.org/10.1001/jama.288.13.1622. [PubMed: 12350193]

52. Roberts CK, Vaziri ND, Barnard RJ. Effect of diet and exercise intervention on blood pressure, insulin, oxidative stress, and nitric oxide availability. Circulation. 2002; 106(20):2530–2532. http://dx.doi.org/10.1161/01.CIR.0000040584.91836.0D. [PubMed: 12427646]

53. Stratton JR, Chandler WL, Schwartz RS, et al. Effects of physical conditioning on fibrinolytic variables and fibrinogen in young and old healthy adults. Circulation. 1991; 83(5):1692–1697. http://dx.doi.org/10.1161/01.CIR.83.5.1692. [PubMed: 1902407]

54. Physical activity and cardiovascular health: NIH consensus development panel on physical activity and cardiovascular health. JAMA. 1996; 276(3):241–246. http://dx.doi.org/10.1001/jama.1996.03540030075036. [PubMed: 8667571]

55. Hinderliter A, Sherwood A, Gullette EC, et al. Reduction of left ventricular hypertrophy after exercise and weight loss in overweight patients with mild hypertension. Arch Intern Med. 2002; 162(12):1333–1339. http://dx.doi.org/10.1001/archinte.162.12.1333. [PubMed: 12076231]

56. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med. 2002; 346(11):793–801. http://dx.doi.org/10.1056/NEJMoa011858. [PubMed: 11893790]

57. Tulppo MP, Makikallio TH, Seppanen T, Laukkanen RT, Huikuri HV. Vagal modulation of heart rate during exercise: effects of age and physical fitness. Am J Physiol. 1998; 274(2 Pt 2):H424–429. [PubMed: 9486244]
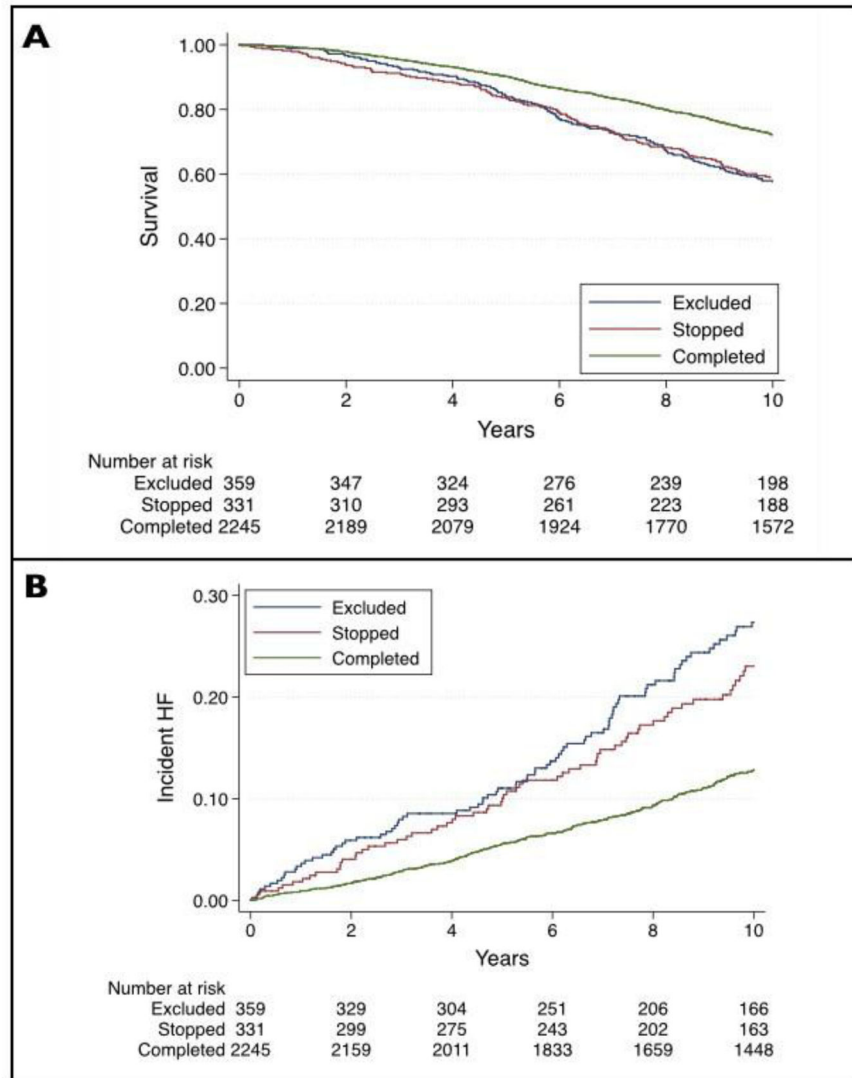
Figure 1.
Kaplan-Meier curve of mortality (A) and incident heart failure (B) according to long distance corridor walk completion status.

Table 1

Baseline Participant Characteristics According to Completion Categories at Baseline

Characteristic	Excluded	Stopped	Completed	p-value[a]
	n=359	n=331	n=2245	
Age, years	74.1 (2.9)	73.9 (2.9)	73.5 (2.8)	**0.001**
Male sex, N (%)	161 (44.8%)	110 (33.2%)	1136 (50.6%)	**<0.001**
Race				**<0.001**
Blacks, N (%)	185 (51.5%)	184 (55.6%)	846 (37.7%)	
Whites, N (%)	174 (48.5%)	147 (44.4%)	1399 (62.3%)	
BMI, kg/m^2	27.9 (5.4)	28.8 (5.8)	27 (4.5)	**<0.001**
Smoking				
Current smokers, N (%)	47 (13.1%)	42 (12.7%)	219 (9.8%)	
Past smokers, N (%)	162 (45.1%)	146 (44.1%)	1011 (45.0%)	
Standing height, mm	1655.0 (96.1)	1631.0 (92.6)	1667.0 (92.9)*	
Leg height, mm	817.0 (67.3)	798.0 (63.4)	818.0 (62.8)**	
Steps to complete first 20 m	-	32.5 (5.76)	29.9 (4.16)	**<0.001**
Physical activity, kcal/kg/week	73.9 (72)	76.3 (71)	86.2 (69)	**<0.001**
Hypertension, N (%)	194 (54.0%)	169 (51.1%)	901 (40.1%)	**<0.001**
Diabetes mellitus, N (%)	69 (19.2%)	67 (20.2%)	295 (13.1%)	**<0.001**
Left ventricular hypertrophy, N (%)	65 (18.1%)	42 (12.7%)	241 (10.7%)	**<0.001**
Coronary heart disease, N (%)	96 (26.7%)	65 (19.6%)	315 (14.0%)	**<0.001**
Cerebrovascular disease, N (%)	31 (8.6%)	34 (10.3%)	133 (5.9%)	**<0.001**
Peripheral vascular disease, N (%)	18 (5.2%)	36 (11.4%)	82 (3.7%)	**<0.001**
Any cardiovascular disease, N (%)	122 (34.0%)	89 (26.9%)	445 (19.8%)	**<0.001**
Pulmonary disease, N (%)	34 (9.5%)	14 (4.2%)	69 (3.1%)	**<0.001**
Depression, N (%)	52 (14.5%)	29 (8.8%)	224 (10.0%)	**0.019**
Systolic blood pressure, mmHg	143 (29)	138 (20)	135 (19)	**<0.001**
Diastolic blood pressure, mmHg	73.5 (15)	71.1 (11)	71.2 (11)	0.15
Heart rate, beats/min	68.3 (14)	68.5 (12)	64.4 (10)	**<0.001**
ECG – major abnormalities, [b] N (%)	113 (31.6%)	87 (26.3%)	422 (18.8%)	**<0.001**
ECG – minor abnormalities, [c] N (%)	75 (21.1%)	60 (18.1%)	358 (16.0%)	0.064
Fasting Glucose, mg/dl	109 (45)	110 (40)	102 (31)	**<0.001**
Albumin, g/dl	3.97 (0.32)	3.97 (0.32)	3.98 (0.31)	0.70
Creatinine, mg/dl	1.09 (0.4)	1.07 (0.54)	1.04 (0.39)	**0.047**
Total cholesterol, mg/dl	203 (41)	207 (37)	203 (38)	0.16

Notes: Continuous variables are presented as mean (SD) or median (25th percentile, 75th percentile); categorical variables are presented as number (%). Boldface indicates statistical significance (*p-value 0.024 for comparison between those who excluded vs. those who completed the test; p-value <0.001 for comparison between those who excluded vs. those who stopped and between those who stopped vs. those who completed the test; **p-value <0.001 for comparison between those excluded or completed the test vs. those who stopped).

[a] Nonparametric test for trend.

[b] Major Q or QS abnormality, major ST or T wave abnormality, left ventricular hypertrophy, atrioventricular conduction defect, ventricular conduction defects, rhythm irregularity.

^{c}Minor Q or QS abnormality or ST or T wave abnormalities.

ECG, electrocardiogram

Table 2

Summary of Responses to LDCW Test Among Completers (n=2,245)

Response variable	Mean (SD)	Median (Q1-Q2)
Walking speed over 20 m, m/s	1.35 (0.24)	1.34 (1.19–1.5)
Distance covered by 2 min, m	155 (26)	155 (138–173)
Time to walk 400 m - complete only, s	331 (61)	323 (289–361)
Speed to walk 400 m, m/s	1.24 (21)	1.24 (1.11–1.38)
Standing SBP, mmHg	138 (21)	136 (124–150)
SBP at the end of 400 m, mmHg	149 (24)	148 (132–164)
Standing DBP, mmHg	77 (13)	78 (70–86)
DBP at the end of 400 m, mmHg	76 (14)	78 (70–86)
Resting heart rate, beats/min	78 (19)	78 (69–87)
Heart rate at the end of 2 min, beats/min	100 (15)	101 (90–111)
Heart rate at the end of the 400 m, beats/min	104 (15)	104 (93–115)
Heart rate at min 2 of recovery, beats/min	87 (15)	88 (77–98)

LDCW, long distance corridor walk test; DBP, diastolic blood pressure; SBP, systolic blood pressure

Table 3

Exercise and Cardiovascular Responses and Association With 10-year Mortality and Heart Failure Incidence Among Completers (n=2,245)

Response variable	Mortality		Incident heart failure	
	Unadjusted HR (95% CI)	Adjusted[a] HR (95% CI)	sHR (95% CI)	Adjusted sHR[a] (95% CI)
Walking speed over first 20 m, per m/s	**0.348 (0.249–0.487)*****	**0.512 (0.285–0.922)***	**0.366 (0.222–0.606)*****	0.448 (0.184–1.089)[b]
Distance covered by 2 min, per m	**0.990 (0.987–0.993)*****	**0.993 (0.988–0.998)****	**0.992 (0.988–0.997)*****	0.998 (0.990–1.005)
Speed to walk 400 m, per m/s	**0.219 (0.149–0.322)*****	**0.280 (0.149–0.526)*****	**0.276 (0.153–0.497)*****	0.505 (0.195–1.307)
Standing SBP, per mmHg	1.001 (0.997–1.006)	1.006 (0.996–1.015)	**1.019 (1.012–1.026)*****	1.005 (0.992–1.019)
SBP at 400 m, per mmHg	1.000 (0.995–1.004)	0.999 (0.994–1.004)	1.000 (0.993–1.007)	1.001 (0.994–1.008)
Standing DBP, per mmHg	0.998 (0.991–1.005)	0.996 (0.988–1.005)	1.007 (0.994–1.020)	0.992 (0.979–1.007)
DBP at 400 m, per mmHg	**1.008 (1.001–1.015)***	1.007 (0.999–1.015)	0.991 (0.981–1.001)	0.994 (0.982–1.006)
Resting heart rate, per beat/min	**1.003 (1.000–1.006)***	1.001 (0.997–1.005)	**1.004 (1.003–1.006)*****	**1.002 (1.000–1.005)***
Heart rate by 2 min, per beat/min	**0.986 (0.980–0.993)*****	0.997 (0.990–1.005)	**0.990 (0.980–1.000)***	0.995 (0.983–1.008)
Heart rate at 400 m, per beat/min	**0.988 (0.982–0.995)*****	0.999 (0.992–1.006)	0.993 (0.983–1.002)	0.998 (0.988–1.009)
Heart rate recovery,[c] per beat/min	**1.014 (1.007–1.022)*****	1.004 (0.996–1.013)	1.003 (0.992–1.015)	0.995 (0.982–1.008)

Note: Boldface indicates statistical significance (*$p<0.05$; **$p<0.01$; ***$p<0.001$).

[a] Adjusted for variables in Table 1 (age, gender, race, BMI, standing height, leg height, steps to complete first 20 meters, smoking, self-reported physical activity, prevalent cardiovascular disease [coronary artery disease, cerebrovascular disease, and peripheral vascular disease], pulmonary disease, diabetes mellitus, hypertension, depression, systolic blood pressure, heart rate, electrocardiographic abnormalities, blood glucose, and serum levels of albumin, creatinine, and cholesterol).

[b] $p=0.07$

[c] Defined as heart rate 2 min after the test minus the heart rate at 400 m.

DBP, diastolic blood pressure; , difference; SBP, systolic blood pressure