Nonexercise Cardiorespiratory Fitness and Mortality in Older Adults

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ABSTRACT

MARTINEZ-GOMEZ, D., P. GUALLAR-CASTILLÓN, P. C. HALLAL, E. LOPEZ-GARCIA, and F. RODRÍGUEZ-ARTALEJO. Nonexercise Cardiorespiratory Fitness and Mortality in Older Adults. *Med. Sci. Sports Exerc.*, Vol. 47, No. 3, pp. 568–574, 2015. **Introduction**: High cardiorespiratory fitness (CRF) is strongly associated with longer life among older adults. CRF can be assessed by exercise-based methods, which are not feasible in most clinical settings. Thus, nonexercise algorithms to estimate CRF have been developed, but whether they predict mortality in older adults is uncertain. **Methods**: A cohort of 1470 men and 1460 women, representative of the Spanish population age ≥60 yr, was established in 2000/2001 and followed up prospectively through 2011. At baseline, nonexercise CRF was estimated with the sex-specific algorithms developed by Jackson et al. Analyses were performed with Cox regression and adjusted for the main confounders. **Results**: During an average follow-up of 9.4 yr, 570 (38.8%) deaths occurred in men and 295 (20.2%) in women. Among men, no association was observed between nonexercise CRF and all-cause mortality. Compared with women in the lowest quartile of CRF, the hazard ratio (95% confidence interval) for all-cause death was 0.81 (0.62–1.06) in the second quartile, 0.68 (0.48–0.95) in the third quartile, and 0.56 (0.36–0.87) in the highest quartile (*P* for trend = 0.004). Results held regardless of age, body mass index, waist circumference, HR, subjective health, functional limitations, and disease status. **Conclusions**: Higher nonexercise CRF was related to lower risk of death in older women but not in men. Because previous research does not support clear sex-specific association, further research is required to assess whether nonexercise CRF predicts mortality in older adults or new algorithms should be developed for this population, with special attention to older men. **Key Words:** CARDIOVASCULAR FITNESS, FITNESS, ELDERLY, SURVIVAL

High cardiorespiratory fitness (CRF) is strongly associated with longer life among older adults (5,17,22,26,28). In addition, there is evidence to suggest that higher CRF is related to better physical and cognitive functions in the elderly (4,17). Assessment of CRF in the clinical setting is potentially important because CRF is a better predictor of adverse cardiovascular outcomes and mortality than physical activity; in addition, high levels of CRF largely negate the adverse effects of traditional cardiovascular risk factors (17). Thus, assessment of CRF may allow for improving risk estimation and, thereby, for modulating the intensity of interventions addressed to control cardiovascular disease and improve survival (17).

Despite these advantages, CRF is not yet routinely assessed in clinical settings (17). CRF, typically expressed as maximal oxygen uptake ($\dot{V}O_{2max}$), can be assessed by direct and indirect methods (1,25). Direct methods require subjects to perform at maximal effort during a graduated exercise on a treadmill or on a cycle ergometer using a respiratory gas analyzer. Indirect methods involve only a submaximal effort, and CRF is estimated from a specific

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physiological response during a standardized protocol (e.g., HR, peak workload, amount of time or distance covered running or walking). However, both types of methods are not feasible in most clinical settings because they require trained staff, expert equipment, sophisticated laboratories, or a large open space as well as a substantial amount of time to perform the protocols correctly (1,25). In addition, these methods may not be safe or appropriate for all older adults because of functional limitations or severe diseases.

Therefore, nonexercise algorithms have been developed for estimating CRF in clinical settings (7,11,12,14,16,20). These algorithms only require data on variables obtained in routine patient care such as gender, age, body mass index (BMI), waist circumference, resting HR, reported physical activity, and tobacco smoking. Higher CRF estimated with nonexercise algorithms has been associated with lower mortality in middle-age individuals (24); however, whether this association also holds in older adults is uncertain. Because earlier algorithms were derived with cross-sectional data in populations that were not very old (i.e., 20–70 yr), new algorithms have been developed from longitudinal studies and have accounted for the age-associated decline in CRF (14). Accordingly, this article aimed to examine whether nonexercise CFR estimated with these new algorithms is associated with all-cause mortality in older adults.

METHODS

Study design and participants. We analyzed data from a cohort of 4008 individuals (1739 men and 2269 women), which was representative of the noninstitutionalized population age ≥60 yr in Spain. The study methods have been reported elsewhere (10). In brief, the study participants were recruited between 2000 and 2001 using probabilistic sampling by multistage clusters. The clusters were stratified according to region of residence and size of municipality. Next, census sections and households were sequentially chosen randomly within each cluster. Finally, study participants were selected in age and sex strata. Subjects who could not participate after 10 failed visits by the interviewer or because of disability, death, institutionalization, or refusal to participate were replaced with other individuals selected with the same sampling procedure. Data were collected by home-based personal interviews and physical examinations performed by trained and certified personnel. The study response rate was 71%. In 2012, we did a computerized search of the National Death Index, which contains information on the vital status of all residents in Spain, to identify all-cause deaths that had occurred in study participants.

A written informed consent was obtained from all study participants and from an accompanying family member. The study was approved by the clinical research ethics committee of the "La Paz" University Hospital in Madrid, Spain.

Assessment of nonexercise CRF. Nonexercise CRF at baseline was estimated in METs (3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$) with the following sex-specific algorithms (14):

$$\begin{aligned}\text{CRF in men (METs)} = {} & 21.2870 + (\text{age} \times 0.1654) - (\text{age}^2 \times 0.0023) \\ & - (\text{BMI} \times 0.2318) - (\text{waist circumference} \times 0.0337) \\ & - (\text{resting HR} \times 0.0390) + (\text{physically active} \times 0.6351) \\ & - (\text{current smoker} \times 0.4263)\end{aligned}$$

$$\begin{aligned}\text{CRF in women (METs)} = {} & 14.7873 + (\text{age} \times 0.1159) - (\text{age}^2 \times 0.0017) \\ & - (\text{BMI} \times 0.1534) - (\text{waist circumference} \times 0.0088) \\ & - (\text{resting HR} \times 0.0364) + (\text{physically active} \times 0.5987) \\ & - (\text{current smoker} \times 0.2994)\end{aligned}$$

The SEE of each algorithm to predict CRF was 1.69 METs for men and 1.53 METs for women (14). Age, BMI, waist circumference, and resting HR are entered as continuous variables, whereas being physically active and being a current smoker are dichotomous variables with a value of 1 when present and 0 when absent.

Weight and height were measured using standardized procedures, and BMI was calculated as weight (kg) divided by height squared (m^2) (10). Waist circumference (cm) was measured with an inelastic belt-type tape at the midpoint between the lowest rib and the iliac crest after breathing out normally (10). Resting HR (bpm) was measured in the right arm at the level of the heart using the OMROM 706/711 automatic blood pressure monitor (OMRON Healthcare UK Ltd., Milton Keynes, United Kingdom) (3). Three HR readings were taken at 2-min intervals, and the mean of the last two readings was used in the analyses (3). Physical activity was assessed with a single question taken from the Spanish National Health Survey (2). Participants rated their leisure time physical activity level as (i) inactive, (ii) occasional physical activity, and (iii) regular physical activity. Those belonging to the categories "occasional" and "regular" were considered physically active (2). Participants also reported whether they never smoked, were former smokers, or are current smokers.

Ascertainment of mortality. The outcome variable was all-cause mortality from the study baseline at 2000/2001 to the end of follow-up at December 31, 2011. Vital status was successfully ascertained for 99.9% of the cohort.

Potential confounders. Potential confounding variables included age, sex, educational attainment, alcohol consumption, blood pressure, hypercholesterolemia, and disease status. Educational attainment was assessed as the highest educational level achieved (no formal education, primary, and secondary or higher). Alcohol consumption was obtained with the frequency–quantity scale used in the Spanish National Health Survey (9). First, participants rated their alcoholic beverage consumption among the following options: abstainer, former drinker, current habitual drinker, or current sporadic drinker. Second, current drinkers also reported the frequency and quantity of beer, wine, and spirits consumed during the previous year to calculate total alcohol intake ($g \cdot d^{-1}$). Blood pressure (mm Hg) at rest was measured six times under standardized conditions using alternatively a calibrated mercury sphygmomanometer and the OMROM 706/711 device; the mean of the six measurements was used in the analyses (3). Participants were also asked the following: has your doctor ever told you whether you have high (blood) cholesterol? If the answer was affirmative, they were considered to have hypercholesterolemia. Finally, the following diseases diagnosed by a physician and reported by the study participant were also recorded: CHD, stroke, diabetes mellitus, hip fracture, and cancer at any site.

Effect modifiers. Given that perceived health and functional limitations may be an intermediate step in the pathway from CRF to mortality, they should not be considered confounders of the study association. In contrast, these variables could modify the effect of CRF because it might be more apparent in those without functional limitation and with good health.

Agility limitation was ascertained with the question "Do you experience any difficulty in bending or kneeling?" (2). Mobility limitation (2) was defined as an affirmative response to any of the following questions: (i) "Do you experience any difficulty in picking up or carrying a shopping bag?"; (ii) "Do you experience any difficulty in climbing one flight of stairs?"; and (iii) "Do you experience any difficulty in walking several city blocks (a few hundred meters)?" Perceived health was assessed using the question "In general, how would you rate your health?" In accordance with the possible replies, health was classified as optimal when it was excellent, very good, or good and as suboptimal when it was fair or poor.

Statistical analysis. Of the 4008 study participants, 64 men age >86 yr and 587 women age >78 yr were excluded because the nonexercise CRF algorithms were developed in a population younger than these ages (14). In addition, 427 subjects were excluded (217 women) because of missing data on study variables. Thus, the analyses were conducted among 2930 individuals (1470 men and 1460 women). All variables were checked for normality of distribution graphically and with standardized tests. The distribution of nonexercise CRF in men and women and according to levels of physical activity also shows a relatively symmetric data set for analysis (see Figure, Supplemental Digital Content 1, http://links.lww.com/MSS/A422, Graphical representation of the distribution of nonexercise CRF in older adults by sex and physical activity levels).

The associations of nonexercise CRF and of their individual components (age, BMI, waist circumference, resting HR, physical activity, and smoking) with total mortality were summarized with sex-specific hazard ratios and their 95% confidence interval (CI) obtained from Cox regression. Nonexercise CRF was entered as a continuous variable so that each hazard ratio represents the mortality risk associated with a 1-MET increase in nonexercise CRF (e.g., approximately increasing walking speed 1 mph; https://sites.google.com/site/compendiumofphysicalactivities/). To avoid linear assumptions, in separate analyses, we also modeled nonexercise CRF in quartiles. The P for linear trend was calculated by modeling the CRF quartiles as a continuous variable. Follow-up duration in number of days was used as the time scale, which started at the date of enrolment in 2000/2001 and continued until date of death or until December 31, 2011. Two Cox models, with progressive adjustment for potential confounders, were fitted. The first model adjusted for age. The second model additionally adjusted for all the potential confounders listed previously.

The analyses were repeated in strata defined by components of nonexercise CRF, as follows: age (<median, ≥median), BMI (<30 $kg \cdot m^{-2}$, ≥30 $kg \cdot m^{-2}$), waist circumference (≤102 cm and >102 cm in men, and ≤88 cm and >88 cm in women), resting HR (<median, ≥ median), physical activity (inactive, active), smoking patterns (nonsmoker, current smoker), and disease status (no disease, one or more diseases). Similar stratifications were performed for the effect modifiers, that is, agility and mobility limitations (no, yes) and perceived health (optimal, suboptimal). We examined whether the study results varied across strata by testing the statistical significance (Wald test) of interaction terms defined as the product of CRF by the stratification variable.

We assessed the assumption of proportionality of hazards both graphically and by testing the significance of the interaction between the main exposure variables and days of follow-up, and we found no evidence of departure from such assumption (all P for interaction > 0.1). All tests were two-sided, and statistical significance was set at $P < 0.05$. The analyses took into account the complex sampling design (used sample weights

TABLE 1. Characteristics of study participants at baseline.

	Men	Women
n	1470	1460
Age (yr)	70.2 ± 6.7	68.6 ± 5.3*
BMI ($kg \cdot m^{-2}$)	28.2 ± 3.9	29.9 ± 4.9*
Waist circumference (cm)	102.5 ± 11.6	97.4 ± 12.3*
Resting HR (bpm)	72.9 ± 12.4	74.7 ± 10.8*
Physically active (%)	65.1	53.8*
Smoking (%)		
Never	28.4	93.7
Former	49.9	3.9
Currently	21.7	2.4*
Educational level (%)		
No education	45.0	55.3
Primary	36.5	35.9
Secondary or higher	18.5	8.8*
Systolic blood pressure (mm Hg)	142.9 ± 19.2	142.4 ± 19.3
Hypercholesterolemia (%)	22.5	30.5*
CHD (%)	2.7	3.0
Stroke (%)	8.6	3.7*
Diabetes mellitus (%)	14.6	16.0
Hip fracture (%)	2.1	2.4
Cancer (%)	1.5	2.1
Alcohol drinking (%)		
Never	24.1	68.0
Former	18.9	5.7
Currently	48.0	26.3*
Alcohol intake ($g \cdot d^{-1}$)	28.2 ± 49.8	3.6 ± 11.1*
Agility limitations (%)	53.4	36.6*
Mobility limitations (%)	34.0	49.8*
Suboptimal subjective health (%)	40.4	52.6*

For continuous variables, values are mean ± SD.
*Denotes statistically significant ($P < 0.05$) differences between the sexes.

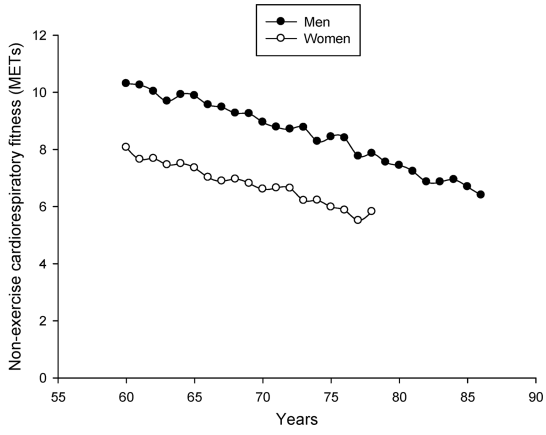

FIGURE 1—Nonexercise CRF levels in older adults by sex and age.

and corrected variances) and were performed with the survey procedure in STATA® version 11.2 for Macintosh.

RESULTS

The main characteristics of the study participants at baseline are shown in Table 1. The mean ± SD of nonexercise CRF was 8.94 ± 1.70 METs (range, 2.43–14.52) in men and 6.84 ± 1.21 METs (range, 1.98–10.25) in women (*P* for sex < 0.001), and sex differences (*P* < 0.001) were found for all ages (Fig. 1).

During an average follow-up of 9.4 yr, 570 (38.8%) deaths occurred in men and 295 (20.2%) occurred in women. Table 2 shows the associations of individual components of nonexercise CRF with all-cause mortality. In men, after adjustment for all potential confounders, age, waist circumference, HR, and smoking were directly associated with mortality whereas physical activity showed inverse association. Interestingly, BMI was linked to lower mortality (hazard ratio, 0.92; 95% CI, 0.89–0.96). Similar results were found in women with the exception of BMI, which showed no association with mortality (hazard ratio, 0.99; 95% CI, 0.96–1.02), and of smoking, which showed tendency to higher mortality, although statistical significance was not reached (hazard ratio, 1.57; 95% CI, 0.84–2.93).

Among men, no association was observed between nonexercise CRF and mortality either when CRF was modeled as a continuous variable (fully adjusted hazard ratio, 1.02; 95% CI, 0.95–1.09) or in quartiles (Fig. 2A). In contrast, among women, nonexercise CRF was inversely associated with mortality (fully adjusted hazard ratio, 0.80; 95% CI, 0.72–0.90; *P* for sex interaction < 0.001). Compared with women in the lowest quartile of CRF, the hazard ratio (95% CI) for all-cause death was 0.81 (0.62–1.06) in the second quartile, 0.68 (0.48–0.95) in the third quartile, and 0.56 (0.36–0.87) in the highest quartile (*P* for trend = 0.004) (Fig. 2B).

To rule out the role of preexisting subclinical disease affecting CRF, we repeated the analysis after excluding the 37 deaths occurring in women during the first 2 yr of follow-up. The resulting mortality risk for a 1-MET increase in nonexercise CRF did not materially change (hazard ratio, 0.79; 95% CI, 0.70–0.89).

In stratified analyses, the inverse association between nonexercise CRF and mortality in women held regardless of age, BMI, waist circumference, HR, physical activity, and disease status (Table 3). In addition, when stratifying by activity limitations and perceived health, no statistically significant interactions were found and, in women, associations were observed in each stratum, except for individuals with mobility limitations (Table 4).

DISCUSSION

We investigated the association of CRF estimated without exercise testing with all-cause mortality in a representative sample of older adults in Spain. Our main result indicates that nonexercise CRF was associated with lower mortality in women but not in men. Specifically, a 1-MET increase in nonexercise CRF was associated with 20% lower mortality among women.

Stamatakis et al. (24) examined the predictive validity of nonexercise CRF algorithms among 32,319 individuals age 35–70 yr from eight British cohorts. They used the nonexercise algorithms developed by Jurca et al. (16) in almost 50,000 individuals age 20–70 yr from three different populations. After adjusting for potential confounders, they found that nonexercise CRF was associated with a 9.4% and 7.1% lower risk of all-cause death per MET in men and women, respectively

EPIDEMIOLOGY

TABLE 2. Sex-specific hazard ratios and their 95% CI for the association of components of nonexercise CRF with all-cause mortality in older adults.

	Men			Women		
	n/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Multivariable-Adjusted[a] Hazard Ratio (95% CI)	*n*/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Multivariable-Adjusted[a] Hazard Ratio (95% CI)
Age (yr)	1470/570	**1.11 (1.09–1.13)**	**1.11 (1.09–1.13)**	1460/295	**1.15 (1.12–1.18)**	**1.15 (1.12–1.17)**
BMI ($kg \cdot m^{-2}$)	1470/570	**0.95 (0.93–0.98)**	**0.92 (0.89–0.96)**	1460/295	**1.03 (1.01–1.06)**	0.99 (0.96–1.02)
Waist circumference (cm)	1470/570	0.99 (0.97–1.01)	**1.01 (1.00–1.02)**	1460/295	**1.02 (1.01–1.03)**	**1.02 (1.01–1.03)**
Resting HR (bpm)	1470/570	**1.01 (1.00–1.02)**	**1.01 (1.00–1.02)**	1460/295	**1.01 (1.00–1.02)**	**1.01 (1.00–1.02)**
Physically active						
No	513/247	1 (reference)	1 (reference)	674/176	1 (reference)	1 (reference)
Yes	957/323	**0.67 (0.55–0.82)**	**0.68 (0.55–0.84)**	786/119	**0.61 (0.49–0.76)**	**0.66 (0.52–0.83)**
Current smoker						
No	1152/427	1 (reference)	1 (reference)	1425/288	1 (reference)	1 (reference)
Yes	318/143	**1.47 (1.16–1.87)**	**1.40 (1.11–1.76)**	35/7	1.27 (0.70–2.32)	1.57 (0.84–2.96)

Statistical significant associations appear in bold font.
[a]Adjusted for age (yr), educational attainment (no education, primary, secondary or higher), alcohol intake ($g \cdot d^{-1}$), former drinking (yes, no), systolic blood pressure (mm Hg), hypercholesterolemia (yes, no), CHD (yes, no), stroke (yes, no), diabetes mellitus (yes, no), hip fracture (yes, no), cancer at any site (yes, no), and the other variables in this table.

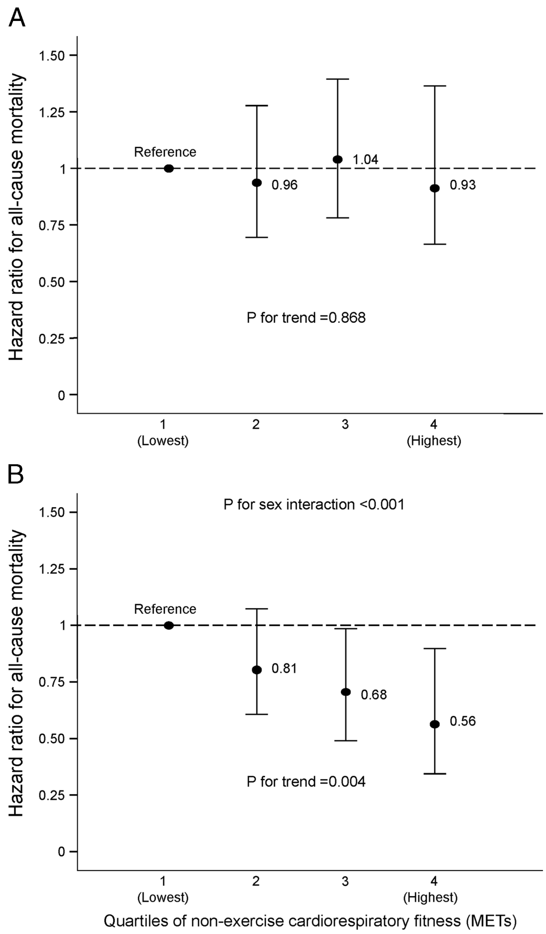

FIGURE 2—Hazard ratios (95% CI) for the association of nonexercise CRF in quartiles with all-cause mortality in older adults by sex, men (A) and women (B). MET, 3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$. Analyses were adjusted for age (yr), educational attainment (no education, primary, secondary or higher), alcohol intake ($g \cdot d^{-1}$), former drinking (yes, no), systolic blood pressure (mm Hg), hypercholesterolemia (yes, no), CHD (yes, no), stroke (yes, no), diabetes mellitus (yes, no), hip fracture (yes, no), and cancer at any site (yes, no).

(24). However, the ability to predict mortality in older adults remained unknown.

As further evidence was needed to determine the validity of nonexercise testing CRF in older adults, Mailey et al. (19) and McAuley et al. (21) examined the construct validity of these nonexercise algorithms in 172 subjects age 60–80 yr. These studies included maximal and submaximal tests and assessed cardiovascular disease and cognitive performance (i.e., cognitive function, brain structure, and subjective memory complaints). Nonexercise CRF showed strong association with maximal ($r = 0.66$) and submaximal ($r = 0.67$) tests and low-to-moderate inverse association with the number of cardiovascular diseases ($r = -0.36$) and cognitive variables ($r = -0.26$ to -0.41). Importantly, the authors found that CRF estimated by nonexercise testing overestimated actual CRF in this population (20,21). This could be due to the fact that CRF declines nonlinearly with age; thus, nonexercise algorithms should account for age-related changes in CRF (13). Jackson et al. (14) further addressed this issue by developing nonexercise CRF algorithms on the basis of longitudinal data from 10,040 men age 20–83 yr and 1325 women age 20–78 yr. Initially, they confirmed that the CRF of both women and men started to decline at about age 45 yr and that the trajectory of change accelerated with aging. Indeed, after about age 60 yr, a linear model systematically underestimated quadratic trend and this error increased with further aging. The new nonexercise CRF algorithms developed by Jackson et al. (14) also have other specific characteristics. First, algorithms are different for men and women. Second, algorithms may use physical activity as a five-level (Likert scale) or a two-level (physically inactive/physically active) variable. Third, algorithms may include either the percentage of body fat (BF) or BMI to estimate CRF.

These characteristics may be important for the interpretation of our findings. Given that nonexercise CRF is calculated separately for men and women, potential errors in previous algorithms due to actual sex differences in CRF (7,11,12,16,20) might be attenuated; in fact, the existence of difference algorithms for men and women may lend some support to our sex-specific findings. In addition, the authors found that algorithms using physical activity based on a two-level variable were only slightly less accurate than those using the five-level variable in middle-age and not very old individuals (14); however, it cannot be ruled out that, among the very old, the five-level variable might improve the performance of the algorithms.

Lastly, we used BMI rather that BF percentage for estimating CRF. Although the estimate error was only slightly lower when using BF percentage instead of BMI in the work by Jackson et al. (14), this may not apply to older adults. BMI, as specified in the algorithms, is usually inversely associated with CRF (14,16), but substantial research has shown that BMI-based overweight may have a null or even an inverse association with mortality in the elderly (6,8,15). This is particularly true in analyses simultaneously including BMI and waist circumference as independent variables (as in the CRF algorithms) because, in this case, BMI mainly reflects lean mass rather than fat mass (18). Because BMI was inversely associated with mortality in men and BMI reduces the estimated nonexercise CRF (see algorithm in Methods), it could have contributed to the null association between nonexercise CRF and mortality in our study. Future research should investigate the ability of nonexercise testing algorithms to predict health risks in older adults using a five-point physical activity scale and BF percentage instead of a two-level physical activity scale and BMI.

Although nonexercise algorithms are easy-to-use and cost-effective tools to assess CRF in clinical settings, our results do not support their predictive validity in community-dwelling older men. Hence, new algorithms for estimating CRF might be necessary in older males. Available options to assess CRF in clinical settings are maximal and submaximal exercise tests (1,25), but their protocols are complex such as that for the "6-min walk test", one of the most widely used submaximal tests for estimating CRF in older adults (27). Other components of health-related physical fitness could be ascertained,

TABLE 3. Sex-specific hazard ratios and their 95% CI for the association of nonexercise CRF with all-cause mortality among older adults in the total sample and stratified by components of the nonexercise CRF.

	Men				Women			
Nonexercise CRF (METs)	*n*/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Fully Adjusted[a] Hazard Ratio (95% CI)	*P* for Interaction	*n*/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Fully Adjusted[a] Hazard Ratio (95% CI)	*P* for Interaction
Total	1470/570	1.00 (0.93–1.07)	1.02 (0.95–1.09)		1460/295	**0.76 (0.69–0.85)**	**0.80 (0.72–0.90)**	
Age < median[b]	757/179	1.01 (0.90–1.14)	1.05 (0.92–1.21)	0.846	718/70	**0.64 (0.52–0.79)**	**0.74 (0.60–0.92)**	0.458
Age ≥ median[b]	713/391	1.00 (0.92–1.09)	1.00 (0.92–1.10)		742/225	**0.81 (0.71–0.92)**	**0.83 (0.73–0.95)**	
BMI, <30 kg·m^{-2}	1000/409	0.90 (0.81–1.01)	0.91 (0.81–1.02)	0.728	819/148	**0.74 (0.59–0.91)**	**0.79 (0.62–0.99)**	0.357
BMI, ≥30 kg·m^{-2}	470/161	1.05 (0.87–1.26)	1.03 (0.86–1.25)		642/147	**0.72 (0.60–0.86)**	**0.75 (0.63–0.90)**	
No abdominal obesity[c]	748/281	1.05 (0.94–1.19)	1.05 (0.93–1.18)	0.279	307/49	**0.66 (0.47–0.95)**	0.68 (0.46–1.00)	0.882
Abdominal obesity[c]	722/288	1.00 (0.90–1.14)	1.03 (0.91–1.16)		1154/246	**0.76 (0.67–0.87)**	**0.79 (0.70–0.90)**	
Resting HR < median[d]	737/270	1.01 (0.91–1.13)	1.03 (0.93–1.15)	0.477	709/132	**0.78 (0.66–0.92)**	0.83 (0.70–1.00)	0.724
Resting HR ≥ median[d]	733/300	1.06 (0.95–1.18)	1.09 (0.97–1.22)		751/163	**0.75 (0.64–0.88)**	**0.76 (0.66–0.89)**	
Physically active	957/323	1.03 (0.93–1.13)	1.05 (0.95–1.16)	0.676	786/119	0.93 (0.79–1.10)	0.98 (0.82–1.17)	0.124
Physically inactive	513/247	1.08 (0.97–1.22)	1.09 (0.97–1.22)		674/176	**0.73 (0.63–0.86)**	**0.78 (0.67–0.91)**	
Non-current smoker	1152/427	0.99 (0.92–1.08)	1.01 (0.93–1.10)	0.060	1425/288	**0.76 (0.69–0.85)**	**0.80 (0.71–0.89)**	
Current smoker	318/143	1.08 (0.93–1.24)	1.08 (0.94–1.25)		35/7	NA	NA	NA
No disease condition	1111/385	0.98 (0.90–1.06)	1.00 (0.91–1.09)	0.877	1114/197	**0.75 (0.66–0.86)**	**0.75 (0.66–0.86)**	**0.048**
With ≥1 disease condition	359/185	1.06 (0.93–1.20)	1.06 (0.93–1.21)		346/98	0.85 (0.71–1.03)	0.86 (0.71–1.04)	

Statistically significant associations appear in bold font.
[a]Adjusted for age (yr), educational attainment (no education, primary, secondary or higher), alcohol intake (g·d^{-1}), former drinking (yes, no), systolic blood pressure (mm Hg), hypercholesterolemia (yes, no), CHD (yes, no), stroke (yes, no), diabetes mellitus (yes, no), hip fracture (yes, no), and cancer at any site (yes, no).
[b]70 yr old in men and 69 yr old in women.
[c]Abdominal obesity was waist circumference >102 cm in men and >88 cm in women.
[d]72 bpm in men and 74 bpm in women.
MET, 3.5 mL O_2·kg^{-1}·min^{-1}; NA, not applicable.

including gait speed and muscular strength, which are affected in the frailty syndrome (23).

Several limitations of this study must be acknowledged. Nonexercise CRF was obtained only at baseline. Although the analyses assumed that the components of nonexercise CRF are relatively stable over time, some changes are still possible and would likely have led to an underestimation of the study association. In addition, information on cause-specific mortality was not available, so we are not aware of the specific pathways (cardiovascular, respiratory, etc.) for the reduced mortality related to nonexercise CRF in women. We could not use the specific physical activity questionnaire used by Jurca et al. (16) and Jackson et al. (14) because it was not available when collecting our data. Finally, the analyses were limited to men ≤86 yr old and women ≤78 yr old (14). We performed additional analyses in individuals above this age, and the results were similar, even though two women obtained CRF scores close to 1 MET and one woman had a negative score.

This study also had several strengths. Specifically, the analyses were adjusted for numerous confounders and the heterogeneous and relatively large sample size made it possible to examine whether the study association varied according to components of nonexercise CRF, educational attainment, and health conditions. Of note, because the association between CRF and lower mortality in women was observed even in those without functional limitations and with good perceived health, these results support that the study findings are not due to reverse causation (i.e., poor health leads to lower CRF and higher mortality).

In conclusion, nonexercise CRF was inversely associated with all-cause mortality in older women. Because the studies that examined the effect of CRF assessed by maximal and submaximal methods with mortality in older adults do not support sex-specific association, further research is required to assess whether nonexercise CRF predicts mortality in older adults, particularly in men. In addition, our findings could

TABLE 4. Sex-specific hazard ratios and their 95% CI for the association of nonexercise CRF with all-cause mortality among older adults stratified by activity limitations and subjective health.

	Men				Women			
Nonexercise CRF (METs)	*n*/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Fully Adjusted[a] Hazard Ratio (95% CI)	*P* for Interaction	*n*/Deaths	Age-Adjusted Hazard Ratio (95% CI)	Fully Adjusted[a] Hazard Ratio (95% CI)	*P* for Interaction
No agility limitations	785/266	0.96 (0.87–1.06)	1.00 (0.90–1.11)	0.661	534/70	**0.76 (0.60–0.95)**	**0.78 (0.61–0.99)**	0.563
With agility limitations	685/304	1.06 (0.96–1.17)	1.06 (0.96–1.18)		926/225	**0.80 (0.70–0.90)**	**0.85 (0.74–0.97)**	
No mobility limitations	970/313	0.99 (0.91–1.09)	1.02 (0.92–1.12)	0.888	740/108	**0.74 (0.62–0.90)**	**0.75 (0.61–0.92)**	0.335
With mobility limitations	500/257	1.04 (0.94–1.15)	1.07 (0.96–1.19)		720/187	**0.81 (0.71–0.93)**	0.88 (0.77–1.01)	
Optimal subjective health	876/276	1.03 (0.93–1.13)	1.04 (0.94–1.14)	0.571	692/97	**0.78 (0.65–0.94)**	**0.80 (0.66–0.97)**	0.886
Suboptimal subjective health	594/294	1.00 (0.90–1.11)	1.01 (0.91–1.12)		768/198	**0.81 (0.70–0.93)**	**0.85 (0.74–0.97)**	

Analyses are not adjusted for the stratification variable. Statistical significant associations appear in bold.
MET, 3.5 mL O_2·kg^{-1}·min^{-1}.
[a]Adjusted for age (yr), educational attainment (no education, primary, secondary or higher), alcohol intake (g·d^{-1}), former drinking (yes, no), systolic blood pressure (mm Hg), hypercholesterolemia (yes, no), subjective health (score), agility limitations (yes, no), mobility limitations (yes, no), CHD (yes, no), stroke (yes, no), diabetes mellitus (yes, no), hip fracture (yes, no), and cancer at any site (yes, no).

also suggest a need for developing new specific algorithms to estimate CRF in older men.

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