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The association between the long-term change in directly measured cardiorespiratory fitness and mortality risk

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Abstract

Introduction: There is a strong inverse association between cardiorespiratory fitness (CRF) and mortality outcomes. This relationship has predominantly been assessed cross-sectionally, however low CRF is a modifiable risk factor, thus assessing this association using a single baseline measure may be sub-optimal. **Purpose:** To examine the association of the long-term change in CRF, measured using cardiopulmonary exercise testing (CPX) with all-cause and disease-specific mortality.

Methods: Participants included 833 apparently healthy men and women (42.9±10.8 years) who underwent two maximal CPXs, the second CPX being ≥ 1 year following the baseline assessment. Participants were followed for 17.7 ± 11.8 years for all-cause, cardiovascular disease (CVD), and cancer mortality. Cox-proportional hazard models were performed to determine the association between the change in CRF, computed as visit 1 (V1) peak oxygen consumption (VO_{2peak} ($ml \cdot kg^{-1} \cdot min^{-1}$)) – visit 2 (V2) VO_{2peak}, and mortality outcomes.

Results: During follow-up, 172 participants died. Overall, the change in CPX-derived CRF was inversely related to all-cause, CVD, and cancer mortality ($p<0.05$). Each 1 $ml \cdot kg^{-1} \cdot min^{-1}$ increase was associated with a 10.8, 14.7, and 15.9% reductions in all-cause, CVD, and cancer mortality, respectively. The inverse relationship between CRF and all-cause mortality remained significant ($p<0.05$) when men and women were examined independently, after adjusting for years since first CPX, baseline VO_{2peak}, and age.

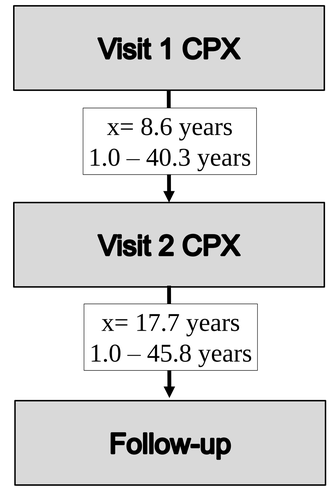
Conclusion: Long-term changes in CRF were inversely related to mortality outcomes, and mortality was better predicted by CRF measured at subsequent examination than baseline CRF. These findings support the recent American Heart Association scientific statement advocating CRF as a clinical vital sign that should be assessed routinely in clinical practice, as well as support regular participation in physical activity to maintain adequate CRF levels across the lifespan.

Introduction

- Cardiorespiratory fitness (CRF) has been shown to be a strong and independent predictor of disease-specific and all-cause mortality[1,2]
- The relationship between CRF and mortality risk has typically been assessed using a single measurement, though some evidence suggests the change in CRF over time influences risk[3]
- However, the current understanding of the association between the change in CRF and mortality risk is based on estimated CRF from a variety of indirect methods[3]
- The strength of this relationship using change in CPX-derived CRF over time in apparently healthy men and women is not well understood

Methods

- Participants included 833 apparently healthy, self-referred adults (552 men, 281 women; 42.9 ± 10.8 years) from the Ball State Adult fitness Longitudinal Lifestyle Study (BALL ST) cohort who were
  - ≥18 years of age
  - Free from CVD and cancer at baseline
- Participants completed two maximal cardiopulmonary exercise tests (CPX) to determine CRF, with the V2 CPX being ≥ 1 year following the V1 CPX
  - Respiratory exchange ratio ≥ 1.00
  - CRF at both tests was indicated by VO_{2peak} defined as the average of the highest two or three consecutive VO_2 values within 2 ml/kg/min, occurring in the last 2 minutes of the CPX
- Participants were followed-up for an average of 17.7 ± 11.8 years for all-cause, CVD, and cancer mortality outcomes using the NDI
- Cox-proportional hazard models were performed to determine the association between the change in CRF, expressed continuously, and mortality outcomes (Table 2)
  - Baseline: adjusted for years since V1 CPX
  - Multivariate: adjusted for years since V1 CPX, V1 CRF, age, sex, examination year, and change in risk factors
- A Wald Chi-square test was used to compare the coefficients estimating the relationship of V1 CRF to V2 CRF with time until death for all-cause mortality (Table 3)



Results

Table 1. Descriptive characteristics of risk factors of the BALL ST Cohort at V1 and V2

	Visit 1	Visit 2
Age (y)	42.9±10.8*	51.6±12.0
Weight (kg)	79.8± 17.6	81.2± 18.9
BMI ($kg \cdot m^{-2}$)	26.3 ± 4.7	27.2± 5.3
Blood glucose ($mg \cdot dL^{-1}$)	95.6±24.9*	99.1±21.5
Total Cholesterol ($mg \cdot dL^{-1}$)	208.1±47.1	203.2± 43.7
SBP/DBP (mmHg)	123/79± 14/10	122/77 ± 22/14
Physical inactivity (%)	54*	41
Smoking (%)	10*	6

Data are expressed as mean ± SD or %.; * p≤0.05

- The mean change in CRF between V1 and V2 was -1.8 $mL \cdot kg^{-1} \cdot min^{-1}$
- Overall, there were 11.6 deaths per 1,000 person years

Table 2. Hazard ratios for all-cause mortality outcomes for BALL-ST cohort according to change in CRF, expressed as both VO_{2peak} and METs

All-cause mortality	Hazard Ratio (95% CI)	% reduction/ $mL \cdot kg^{-1} \cdot min^{-1}$	% reduction / MET
	All		
Baseline	0.923 (0.953 – 0.972)	7.7	27.0
Multivariate	0.892 (0.843 – 0.943)	10.8	37.8
	Men		
Baseline	0.934 (0.911 – 0.957)	6.6	23.1
Multivariate	0.899 (0.842 – 0.960)	10.1	35.4
	Women		
Baseline	0.897 (0.929 – 0.999)	10.3	36.1
Multivariate	0.922 (0.793 – 1.072)	7.8	27.3

Results shown as HR (95% CI)
Baseline: adjusted for years since V1 CPX
Multivariate: adjusted for years since V1 CPX, V1 CRF, age, sex, examination year, and change in risk factors
Sex-specific models controlled for the same covariates with the exclusion of sex

Table 3. Comparison of V1 CRF and V2 CRF as predictors of mortality outcomes

	Absolute parameter estimate CPX1	Absolute parameter estimate CPX2	p
Model 1	0.014	0.052*	0.001
Model 2	0.006	0.029*	0.001

*Comparison of the coefficients for V1 CRF to V2 CRF Model 1 run unadjusted; Model 2 adjusted for years since V1 CPX, V1 CRF, age, and sex

- CRF was inversely associated with risk for disease-specific mortality
  - CVD: 15% lower risk / 1 $mL \cdot kg^{-1} \cdot min^{-1}$ increase
  - Cancer: 16% lower risk / 1 $mL \cdot kg^{-1} \cdot min^{-1}$ increase
- The Wald Chi-square test of equality (**Table 3**) found V2 CRF to be a significantly stronger predictor of all-cause mortality than V1 CRF ($p<0.05$)

Conclusions

- Long-term changes (≥ 1 year) in CRF were inversely related to mortality outcomes, and mortality was better predicted by CRF measured at subsequent examination than baseline CRF
- Significant changes in mortality outcomes were seen even with small changes in CRF (1 $mL \cdot kg^{-1} \cdot min^{-1}$) and were independent of changes in traditional risk factors
- These findings support the recent American Heart Association scientific statement advocating CRF as a clinical vital sign[4], as well as support regular participation in physical activity to maintain adequate CRF levels across the lifespan

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