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Research Letter

High fitness levels attenuate the increased risk of hypertension due to low socioeconomic status in middle-aged men: a cohort study

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Running title: Socioeconomic status, cardiorespiratory fitness, and hypertension

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Hypertension (HTN) is the most common modifiable risk factor for cardiovascular disease, the leading cause of mortality globally. Several studies have documented a relationship between low socioeconomic status (SES) and increased risk of HTN.¹ Pathways underlying the relationship include the presence of factors that are strongly related to lower SES such as lower levels of education, unhealthy lifestyles such as excessive alcohol consumption, limited access to health care, and higher prevalence of comorbid conditions.¹ The health benefits of physical activity (PA) are well established and these include the prevention of vascular diseases such as HTN.² Cardiorespiratory fitness (CRF), considered to be the gold standard for assessing aerobic exercise capacity, is an indicator of cardiopulmonary function and can be increased through increased PA and exercise training.³ Cardiorespiratory fitness is an established and independent risk marker for vascular outcomes including hypertension.⁴ There is increasing evidence showing that higher levels of CRF can attenuate the increased risk of adverse outcomes due to other risk factors. For instance, we have previously shown that high CRF levels can attenuate (i) the increased risk of mortality due to SES,⁵ (ii) the increased risk of sudden cardiac death due to low SES,⁶ (iii) the increased risk of pneumonia due to inflammation,⁷ and (iv) the increased risk of chronic obstructive pulmonary disease due to low SES.⁸ Several reports have also observed that the association of obesity with adverse outcomes is reduced on accounting for CRF levels.⁹

Considering the overwhelming evidence, we hypothesized that high fitness levels would attenuate the increased risk of HTN due to low SES. In this context, we evaluated the separate and joint effects of SES and CRF on incident HTN risk using a cohort of 1,612 middle-aged Caucasian men without a history of HTN at baseline.

METHODS

Participants utilized in the current analysis were part of the Kuopio Ischemic Heart Disease (KIHD) prospective cohort study. The cohort comprised a representative sample of middle-aged men aged 42-61 yr recruited in eastern Finland, who underwent baseline examinations between March 1984 and December 1989. The Research Ethics Committee of the University of Eastern Finland approved the study protocol and written informed consent was obtained from all participants. Socioeconomic status was assessed using self-reported questionnaires, which involved a summary index that combined measures of income, education, occupational prestige, material standard of living and housing conditions.⁵ Briefly, the items for each indicator were scored and summed. For material standard of living, a material possession index was based on self-reports of ownership of 12 items (color TV, video tape recorder, freezer, dish washer, car, motorcycle, telephone, summer cottage, house trailer, motorboat, sailing boat, and ski mobile). An individual score was derived about the ownership of the 12 items and divided by the total number of item responses. The composite SES index ranged from 0 to 25, with higher values indicating lower SES. Cardiorespiratory fitness, measured by peak oxygen uptake (VO_{2peak}), was assessed using respiratory gas exchange analyzers (Medical Graphics, MCG, St. Paul, Minnesota) during progressive cycle ergometer exercise testing to volitional fatigue.^{5, 6} For this analysis, men with a prevalent history of HTN (defined as having a clinical diagnosis of HTN, systolic blood pressure (SBP) ≥ 140 mm Hg and/or diastolic blood pressure (DBP) ≥ 90 mm Hg, or use of anti-hypertensive medication at baseline) were excluded. We included all incident cases of HTN that occurred from study entry through to 2018.¹⁰ Cox proportional hazards models were used to estimate multivariable-adjusted hazard ratios (HRs) with 95% CIs for incident HTN. To maintain consistency with previous reports,^{5, 11} the exposures (SES and CRF) were categorized into low and high levels based on the median values. Cardiorespiratory fitness was also modeled as a continuous variable, given evidence of a linear relationship with HTN. Evaluation of the joint association of SES and CRF with risk of hypertension was based on the

following four combinations: high SES-low CRF (reference comparison); low SES- low CRF; high SES-high CRF; and low SES-high CRF. Stata version MP 16 (Stata Corp, College Station) was employed for all analyses.

RESULTS

The overall mean \pm SD age of men at baseline was 53 \pm 5 yr. The mean \pm SD of SES and CRF was 8.32 \pm 4.29 and 31.5 \pm 8.0 ml/kg/min, respectively. During a median (interquartile range) follow-up of 25.9 (17.8-30.9) yr, 394 (24.4%) incident HTN cases were recorded. Compared to men with high SES, low SES was associated with an increased risk of HTN independent of age 1.40 (95% CI: 1.15-1.72) (Figure: Model 1), which was minimally attenuated on further adjustment for SBP, body mass index, smoking status, history of type 2 diabetes, family history of HTN, total cholesterol, high-density lipoprotein cholesterol, alcohol consumption, and PA (Figure: Model 2). The association remained similar on further adjustment for CRF 1.33 (95% CI: 1.08-1.64). On adjustment for the covariates as above, high CRF was associated with a decreased risk of HTN compared with low CRF 0.74 (95% CI: 0.60-0.92) (Figure: Model 2), which remained similar on additional adjustment for SES 0.75 (95% CI: 0.60-0.93).

Compared with men with high SES-low CRF, high SES-high CRF was associated with a decreased risk of HTN in multivariable analysis 0.72 (95% CI: 0.54-0.95), with no evidence of an association for low SES-high CRF and HTN risk 0.99 (95% CI: 0.74 - 1.34) (Figure: Model 2). For every 1SD increase in CRF, HRs (95% CIs) for HTN were 0.78 (0.67-0.92) for men with high SES and 0.88 (0.74-1.04) for men with low SES (*P*-value for interaction=.31).

DISCUSSION

In this general population-based study of middle-aged Finnish men, we have confirmed previously reported associations of low SES with increased HTN risk and high CRF with reduced HTN risk. Evaluation of the joint associations suggests that increased CRF levels may attenuate the increased risk of HTN attributed to low SES. There was no statistically significant evidence that SES modified the association between high CRF levels and decreased HTN risk. These findings add to the existing evidence on the beneficial effects of fitness, its role as a major determinant of clinical outcomes, and its ability to offset the harmful consequences of other risk factors.

Though half of the variation in CRF is attributed to heritability, a physically active lifestyle with aerobic PA being a major component, confers good CRF.³ There is a consistent, temporal, and dose-dependent relationship between PA and the development of HTN.² The mechanistic pathways underlying the relationship between PA and reduction in blood pressure are not fully understood yet. However, the following mechanisms among many others, have been proposed: (i) decreased vascular resistance, arterial stiffness, inflammation, oxidative stress, and renin-angiotensin system activity and (ii) improved endothelial function, insulin sensitivity, sodium handling, renal function, and angiogenesis.² Despite the development of guidelines and recommendation of several strategies for promoting PA, levels are still low in the general population. For people with low SES, more education is needed and accessibility to PA resources should be widened.

The strengths of this evaluation include the novelty, the prospective cohort design, and the use of an objective gold standard measure of CRF. The limitations were the use of self-reported questionnaires in assessing SES and findings not generalizable to women. There was a potential for regression dilution bias due to the use of only baseline measurements of the exposures and the long follow-up duration. Given that regression dilution bias is known to underestimate the true strength of the association between an exposure and outcome, the true associations may be stronger than what we have demonstrated.

CONCLUSIONS

In a general male Finnish population, both SES and CRF were each independently associated with the risk of HTN. However, high CRF may attenuate the increased risk of HTN related to low SES.

Acknowledgements

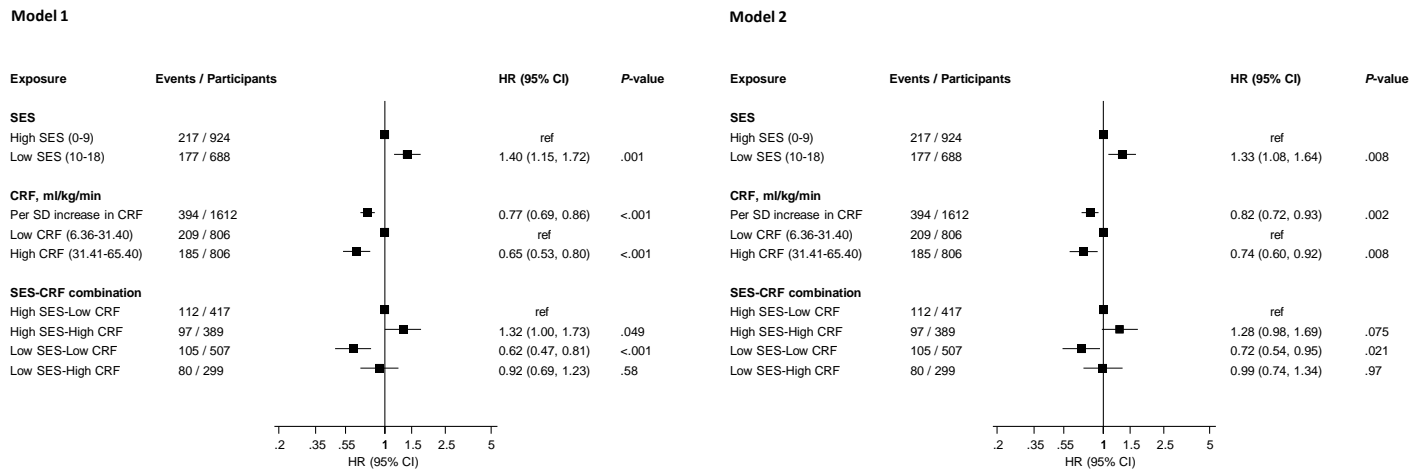
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Figure title and legend

Figure. Separate and combined associations of socioeconomic status and cardiorespiratory fitness with risk of hypertension



CRF, cardiorespiratory fitness; HR, hazard ratio; ref, reference; SD, standard deviation; SES, socioeconomic status

Cut-offs for SES and CRF were based on the median values

Model 1: Adjusted for age

Model 2: Model 1 plus systolic blood pressure, body mass index, smoking status, history of type 2 diabetes, family history of hypertension, total cholesterol, high-density lipoprotein cholesterol, alcohol consumption, and physical activity

Table. Separate and joint associations of socioeconomic status and cardiorespiratory fitness with risk of hypertension

Exposure categories	Events/ Total	Model 1		Model 2		Model 3	
		HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Socioeconomic status							
High SES	217 / 924	ref		ref		ref	
Low SES	177 / 688	1.40 (1.15-1.72)	.001	1.33 (1.08-1.64)	.008	1.30 (1.06-1.60)	.013
CRF (ml/kg/min)							
Per SD increase in CRF	394 / 1612	0.77 (0.69-0.86)	<.001	0.82 (0.72-0.93)	.002	0.83 (0.73-0.94)	.003
Low CRF	209 / 806	ref		ref		ref	
High CRF	185 / 806	0.65 (0.53-0.80)	<.001	0.74 (0.60-0.92)	.008	0.75 (0.60-0.93)	.009
Socioeconomic status and CRF (ml/kg/min) combination							
High SES-Low CRF	112 / 417	ref		ref		NA	
Low SES- Low CRF	97 / 389	1.32 (1.00-1.73)	.049	1.28 (0.98-1.69)	.075	NA	
High SES-High CRF	105 / 507	0.62 (0.47-0.81)	<.001	0.72 (0.54-0.95)	.021	NA	
Low SES-High CRF	80 / 299	0.92 (0.69-1.23)	.58	0.99 (0.74-1.34)	.97	NA	

CI, confidence interval; CRF, cardiorespiratory fitness; HR, hazard ratio; NA, not applicable; ref, reference; SD, standard deviation; SES, socioeconomic status

Cut-offs for SES and CRF were based on the median values

Model 1: Adjusted for age

Model 2: Model 1 plus systolic blood pressure, body mass index, smoking status, history of type 2 diabetes, family history of hypertension, total cholesterol, high-density lipoprotein cholesterol, alcohol consumption, and physical activity

Model 3: Model 2 plus CRF for SES and SES for CRF