Association of Cardiorespiratory Fitness And Body Mass Index with Incident Restrictive Lung Disease

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ABSTRACT

PURPOSE: To estimate the independent and joint associations of cardiorespiratory fitness (CRF) and body mass index (BMI) on the incidence of restrictive lung disease (RLD), which has limited data.

METHODS: This was a prospective study of 12,772 individuals (mean age of 44 years) enrolled in the Aerobics Center Longitudinal Study (ACLS). Participants had at least two visits between 1974 and 2003, and were free from obstructive or restrictive lung disease, cardiovascular disease, and cancer at baseline. CRF (METs) was measured using a maximal treadmill test and was categorized into quintiles. CRF was further dichotomized into "fit" and "unfit" categories (lowest 20% and highest 80% of CRF, respectively) and combined with BMI to evaluate the joint associations. RLD was defined as the ratio of the forced expiratory volume in 1-second (FEV_1), forced vital capacity (FVC) ≥ lower limit of normal (LLN), and an FVC < LLN. Cox proportional hazard models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (95% CIs) of RLD by quintiles of CRF, adjusting for potential confounders.

RESULTS: There were 974 (7.6%) cases of RLD over an average follow-up of 6.8 years. Compared with the first quintile of CRF (the least fit), the fully adjusted HRs (95% CIs) for incident RLD were 0.67 (0.55 - 0.81), 0.52 (0.42 - 0.64), 0.47 (0.38 - 0.58), and 0.34 (0.26 - 0.44) for the second, third, fourth, and fifth quintiles of CRF, respectively, after adjusting for potential confounders including smoking status, physical activity, BMI, and other lifestyle and health conditions. Compared to normal weight, HRs (95% CIs) in overweight and obesity were 0.93 (0.80 - 1.08) and 1.07 (0.85 - 1.36), respectively, after adjusting for potential confounders, including CRF. In the joint analysis, those who were both "fit and normal weight" (upper 80% of CRF and BMI < 25 kg/m^2) had the lowest risk of RLD among all exposure combinations (adjusted HR [95% CI]: 0.50 [0.37 - 0.67]).

CONCLUSIONS: Cardiorespiratory fitness has a significant and independent association with incident RLD in middle-aged adults. Higher fitness and normal BMI was associated with the lowest risk of developing RLD.

INTRODUCTION

High cardiorespiratory fitness (CRF) is protective against a range of morbidities, and data suggests this protection extends to **respiratory disease.** High body mass index (BMI) is a known risk factor of **restrictive lung disease** (RLD), a chronic condition characterized by a progressive decline in **lung volume.** However, the **independent** and **joint associations** of **CRF** and **BMI** on **incident RLD** are unknown.

METHODS

PARTICIPANTS: 12,772 individuals (mean age of 44 years) enrolled in the Aerobics Center Longitudinal Study (ACLS) who were without RLD, asthma, chronic obstructive pulmonary disorder, cancer, or cardiovascular disease at baseline.

CRF: Time to complete a maximal treadmill test, with participants subsequently categorized into sex and age-specific quintiles (based on the ACLS data as a whole)

BMI: Body mass in kilograms (kg) divided by height in meters squared (m^2).

RLD: Assessed by spirometry and defined using the cut-points indicated above.

STATISTICAL ANALYSIS

Baseline characteristics were analyzed using **Chi-squared** (χ_2) for categorical variables and **general linear models** for continuous variables. The independent and joint associations of CRF and BMI on incident RLD were determined using **cox proportional hazard models** (adjusting for potential confounders). Data were analyzed using **SAS version 9.4** (SAS Institute Inc).

RESULTS

Table 1. Participant characteristics at baseline.

Characteristic	All (n = 12 772)	Cases (n = 974)	Non-cases (n = 11 798)	*P* Value[a]
Age, mean (SD), y	43.8 (9.3)	43.1 (8.8)	43.8 (9.3)	0.010
Women, No. (%)	2086 (16.3)	134 (13.8)	1952 (16.6)	0.024
Height, mean (SD), cm	176.7 (8.4)	177.2 (7.9)	176.6 (8.4)	0.040
BMI, mean (SD), kg/m^2	25.3 (3.5)	25.6 (3.9)	25.3 (3.4)	0.005
Smoking status, No. (%)				
Never	6867 (53.8)	514 (52.8)	6362 (53.9)	0.002
Previous	4116 (32.2)	288 (29.6)	3828 (32.5)	
Current	1780 (13.9)	172 (17.7)	1608 (13.6)	
Heavy alcohol drinking[b], No. (%)	2279 (17.8)	153 (15.7)	2126 (18.0)	0.070
Treadmill time, mean (SD), mins	17.9 (4.9)	16.5 (4.8)	18.0 (4.9)	**<.0001**
Maximal METs, mean (SD)	11.6 (2.4)	11.0 (2.2)	11.7 (2.4)	**<.0001**
Meets aerobic physical activity guidelines[c], No. (%)	4940 (38.7)	259 (26.6)	4681 (39.7)	**<.0001**
Total physical activity, mean (SD), MET·h^{-1}·wk^{-1}	668.7 (1102.4)	442.5 (880.7)	687.3 (1116.7)	**<.0001**
Peak FEV_1, % predicted	3.8 (0.7)	3.5 (0.7)	3.8 (0.7)	**<.0001**
Peak FVC, % predicted	4.8 (0.9)	4.4 (0.8)	4.9 (0.9)	**<.0001**
Peak FEV_1/FVC	0.79 (0.07)	0.78 (0.07)	0.79 (0.07)	0.427
Diabetes, No. (%)	532 (4.2)	49 (5.0)	483 (4.1)	0.160
Hypertension, No. (%)	7644 (59.9)	659 (67.7)	6985 (59.2)	**<.0001**

Abbreviations: No., number; SD, standard deviation; BMI, body mass index; MET, metabolic equivalent; MET·h^{-1}·wk^{-1}, weekly energy expenditure in MET hours; FEV_1, Forced expiratory volume in 1-second; FVC, forced vital capacity; FEV_1/FVC, the ratio between FEV_1 and FVC.
[a]*P* value for the comparison between cases and non-cases.
[b]Heavy drinking defined as >7 alcoholic drinks/week for women, and >14 alcoholic drinks/week for men.
[c]Meeting aerobic physical activity guidelines is as ≥500 MET-min/week.

Table 2. Cox proportional hazard regression for the independent associations between cardiorespiratory fitness (CRF) and body mass index (BMI) on restrictive lung disease (RLD).

	Cases (%)	No. of participants	RLD, HR (95% CI)		
			Model 1[a]	Model 2[b]	Model 3[c]
CRF[d]					
Q1 (Least fit)	218 (14.8)	1472	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
Q2	219 (9.6)	2292	**0.64 (0.53-0.77)**	**0.66 (0.54-0.79)**	**0.67 (0.55-0.81)**
Q3	183 (7.3)	2505	**0.48 (0.39-0.59)**	**0.50 (0.41-0.61)**	**0.52 (0.42-0.64)**
Q4	208 (6.5)	3224	**0.43 (0.35-0.52)**	**0.45 (0.37-0.56)**	**0.47 (0.48-0.58)**
Q5 (Most fit)	146 (4.5)	3279	**0.30 (0.24-0.37)**	**0.32 (0.25-0.41)**	**0.34 (0.26-0.44)**
P for linear trend			**<.0001**	**<.0001**	**<.0001**
BMI[e]					
Normal weight	466 (7.4)	6281	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
Overweight	400 (7.4)	5387	**1.19 (1.03-1.36)**	1.10 (0.95-1.27)	0.93 (0.80-1.08)
Obese	108 (9.8)	1104	**1.92 (1.55-2.38)**	**1.63 (1.31-2.03)**	1.07 (0.85-1.36)
P for linear trend			**<.0001**	**<.0001**	<.972

Abbreviations: HR, hazard ratio; CI, confidence interval.
[a]Model 1 was adjusted for sex, age (years), and examination year.
[b]Model 2 was adjusted for Model 1 plus smoking status (never, former, current), heavy alcoholic intake (yes or no), meeting the aerobic physical activity guidelines (yes or no), diabetes (yes or no), hypertension (yes or no).
[c]Model 3 was adjusted for Model 2 plus CRF (METs) or BMI (kg/m^2).
[d]Quintiles of CRF were based on the distribution of the age and sex distribution of treadmill duration for the entire Aerobic Center Longitudinal Center cohort.
[d]Normal weight (BMI <25kg/m^2), overweight (BMI 25-29.9 kg/m^2), and obese (BMI ≥30 kg/m^2).

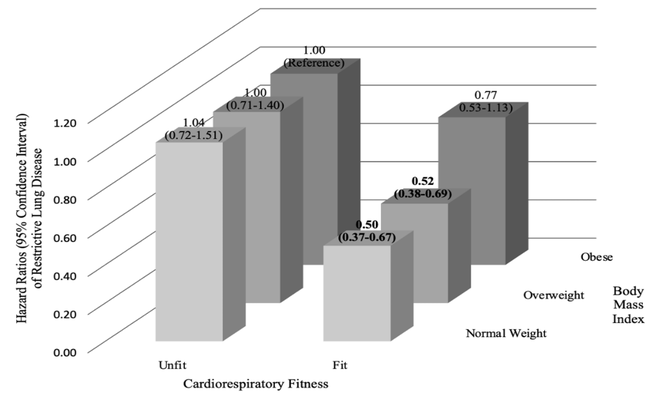

Figure 1. Joint Associations of Cardiorespiratory Fitness and Body Mass Index with restrictive lung disease. Participants were divided into six groups based on combined categories of cardiorespiratory fitness (unfit or fit) and body mass index (normal weight, overweight, or obese), respectively. "Unfit" was the lower 20% of cardiorespiratory fitness, and "Fit" was the upper 80% of cardiorespiratory fitness. Normal weight was body mass index < 25.0 kg/m^2, overweight was 25.0-29.9 kg/m^2, and obese was ≥30.0 kg/m^2. The model was adjusted for sex, age (years), examination year, smoking status (never, former, current), heavy alcohol intake (yes or no), meeting the aerobic physical activity guidelines (yes or no), diabetes (yes or no), hypertension (yes or no). The number of participants (cases of restrictive lung disease) in the "obese and unfit," "obese and fit," "overweight and unfit," "overweight and fit," "normal weight and unfit,", and "normal weight and fit" groups were 408 (53), 696 (55), 675 (99), 4712 (301), 389 (66), and 5892 (400), respectively.

CONCLUSIONS

We found a significant and inverse association between CRF at baseline and incident RLD, independent of BMI. In a joint analysis, we demonstrated that those who were 'fit and normal weight' had the lowest risk of incident RLD relative to those who were 'unfit and obese' (referent). Maintaining a healthy body weight in addition to a good level of fitness (relative to age and sex-specific norms) may prove beneficial to respiratory health in middle-age.