Research Paper

Influence of cardiovascular risk burden on pulmonary function trajectory: role of physical and social activities

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Keywords: Framingham general cardiovascular risk score, pulmonary function, physical activity, social activity, community-based cohort study
Received: March 18, 2022 **Accepted:** July 21, 2022 **Published:** August 4, 2022

ABSTRACT

The impact of cardiovascular risk burden on long-term trajectories of pulmonary function (PF) remains unclear. We examined the association of cardiovascular risk burden assessed by Framingham general cardiovascular risk score (FGCRS) with PF decline and explored whether cardiovascular diseases (CVD), physical and social activities play a role in the association. Within the Rush Memory and Aging Project, 1,442 participants (mean age:79.83) were followed up to 22 years. FGCRS at baseline was calculated and categorized into tertiles. Composite PF was measured annually based on peak expiratory flow, forced expiratory volume in one second, and forced vital capacity. We found that the highest FGCRS was associated with faster PF decline (β: -0.013, 95% CI: -0.023 to -0.003) compared with the lowest FGCRS. There were significant interactions between higher FGCRS and low level of physical/social activity (β: -0.014, 95% CI: -0.026 to -0.003)/(β: -0.020, 95% CI:-0.031 to -0.009) or CVD(β: -0.023, 95% CI:-0.034 to -0.011) compared to the low FGCRS with high level of physical/social activity or without CVD (P-interaction<0.05). Our results suggest that higher cardiovascular risk burden is associated with a faster PF decline, especially among people with CVD. High level of physical activity and social activity appears to mitigate this association.

INTRODUCTION

Aging is inevitably attended by a decline in pulmonary function (PF), owing to various factors, including lung elasticity damage and respiratory muscle weakness [1]. To evaluate the respiratory system function, PF is comprehensively measured by forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF) [2]. Furthermore, low PF has been linked to decreased general health and quality of life and increased all-cause mortality in older adults [3–5].

Growing evidence suggests that traditional cardiovascular risk factors, including smoking, hypertension, dyslipidemia, and diabetes mellitus, may be linked to poor FEV1, FVC, or PEF, respectively

[6–9], though with inconsistent results [10, 11]. Cardiovascular risk factors are well known to be interrelated, and therefore, a comprehensive indicator makes it possible to evaluate the overall cardiovascular burden. The Framingham general cardiovascular risk score (FGCRS), combining age and sex with traditional cardiovascular risk factors, is a prediction scoring algorithm used to thoroughly assess the burden of cardiovascular risk and the likelihood of developing cardiovascular disease (CVD) [12]. However, there are still unanswered questions regarding whether and to what extent FGCRS may affect the long-term trajectories of PF.

Although the incidence of cardiovascular disease in older adults is increasing, modifiers of its association with PF have not been well studied. Previous studies have shown that poorer physical activity [13, 14] and social activity [15] are related to poorer PF among older adults. Consequently, it is essential to further explore whether physical and social activities have a moderating effect on the association of FGCRS with PF decline.

In the current study, using data from the Memory and Aging Project (MAP), we 1) examine the relationship of FGCRS-assessed cardiovascular risk burden with long-term trajectories of PF, and 2) explore the role of CVD, physical and social activities in the association between FGCRS and PF.

RESULTS

Baseline characteristics

Among the 1,442 participants with a mean age of 79.83±7.47 years, the range of FGCRS was 4-28 at baseline. Participants with the highest FGCRS were older, had higher proportions of males and smokers, and had lower educational attainment, physical activity, social activity, and HDL-C, compared to those with the lowest FGCRS. Furthermore, those with the highest FGCRS also tended to have higher BMI and SBP, and have hypertension, diabetes, stroke, and heart diseases (Table 1).

Association of FGCRS with PF

During a median follow-up of 7 years, when FGCRS was treated as a continuous variable, higher FGCRS was associated with a faster decline in PF (β: -0.002, 95% CI: -0.003 to -0.000) and a faster decline in FVC (β: -0.001, 95% CI: -0.002 to -0.000) and FEV1 (β: -0.001, 95% CI: -0.002 to -0.000) over time.

Participants with middle/highest FGCRS experienced an accelerated decline in PF (β: -0.010, 95% CI: -0.020 to -0.001)/ (β: -0.013, 95% CI: -0.023 to -0.003) and FVC (β: -0.008, 95% CI: -0.014 to -0.001)/ (β: -0.009, 95% CI: -0.016 to -0.002), compared to those with lowest FGCRS. Moreover, participants with highest FGCRS had a faster decline in FEV1 (β: -0.008, 95% CI: -0.014 to -0.002), compared to those with lowest FGCRS. The association between high FGCRS and PEF was not significant (Table 2 and Figure 1). The results of covariates were expressed in Supplementary Table 3.

Role of CVD, physical activity, and social activity in the FGCRS-PF association

As middle and highest FGCRS were both related to PF decline, they were combined into one group as high FGCRS in the joint effect analyses. In joint effect analyses (Table 3), there were significant interactions between higher FGCRS and low level of physical/social activity (β: -0.014, 95% CI: -0.026 to -0.003, *P*-interaction= 0.048)/ (β: -0.020, 95% CI: -0.031 to -0.009, *P*-interaction= 0.016) or CVD (β: -0.023, 95% CI: -0.034 to -0.011, *P*-interaction= 0.017) compared to the low FGCRS with high level of physical/social activity or without CVD. However, there was no interaction between FGCRS and smoking on PF ($P > 0.05$) (Supplementary Table 4).

Sensitivity analysis

The results were not much altered when we repeated the analyses by excluding PF observations at baseline and within the first 2 years during the follow-up (Supplementary Table 5).

DISCUSSION

In the long-term population-based longitudinal cohort study among the elderly, we found that 1) higher FGCRS-assessed cardiovascular risk burden was related to faster decline of composite PF, FVC, and FEV1, especially among people with CVD, and 2) there were significant interactions between FGCRS and physical/social activity, and high levels of physical and social activities could mitigate PF decline related to higher FGCRS. Our findings reveal the adverse effect of vascular risk burden on pulmonary health and highlight the importance of active life in preventing pulmonary dysfunction among older people with a higher vascular risk burden.

Previous studies suggest that single cardiovascular risk factors (e.g., smoking, hypertension, diabetes, and dyslipidemia) are related to decreased lung function, with some inconsistent results [6–9]. A cohort study suggested that smoking is not associated with FVC decline [10]. In addition, some longitudinal studies

Table 1. Characteristics of the study population by tertiles of the Framingham general cardiovascular risk score (FGCRS) at baseline (N =1,442).

Characteristics	FGCRS*			*P*-value
	Lowest (N=535)	Middle (N=442)	Highest (N=465)	
Age, yrs	77.67 ± 8.52	80.99 ± 6.74	81.20 ± 6.19	<0.001
Female	474 (88.60)	327 (73.98)	275 (59.14)	<0.001
Education, yrs	15.11 ± 2.99	14.75 ± 3.23	14.66 ± 3.22	0.025
BMI, kg/m^2	26.75 ± 5.25	27.39 ± 5.44	28.13 ± 4.98	<0.001
Alcohol consumption, g	1.08 (0.00, 6.04)	0.00 (0.00, 5.83)	0.00 (0.00, 5.18)	0.096
Smoking status				0.033
Never	308 (57.57)	274 (61.99)	276 (59.35)	
Former smoker	220 (41.12)	160 (36.20)	171 (36.77)	
Current smoker	7 (1.31)	8 (1.81)	18 (3.87)	
SBP, mm Hg	123.14 ± 12.59	134.52 ± 14.28	147.20 ± 16.36	<0.001
HDL-C, mg/dl	65.37 ± 16.72	60.99 ± 18.22	53.44 ± 18.01	<0.001
TC, mg/dl	189.57 ± 34.73	193.95 ± 43.78	191.85 ± 46.62	0.576
Pulmonary function	-0.02 (-0.61, 0.52)	-0.12 (-0.63, 0.56)	0.05 (-0.54, 0.69)	0.132
FVC	0.09(-0.53,0.79)	0.01(-0.54,0.72)	0.19(-0.48,0.98)	0.141
FEV1	0.08(-0.48,0.80)	0.04(-0.52,0.78)	0.19(-0.44,0.99)	0.196
PEF	0.03(-0.59,0.60)	-0.01(-0.60,0.62)	0.03(-0.59,0.60)	0.452
Hypertension	242 (45.23)	306 (69.23)	401 (86.24)	<0.001
Diabetes	19 (3.55)	39 (8.82)	146 (31.40)	<0.001
Stroke	32 (6.71)	34 (8.29)	54 (12.19)	0.012
Congestive heart failure	20 (3.85)	26 (6.24)	17 (3.97)	0.166
Heart diseases	29 (5.42)	43 (9.73)	60 (12.93)	<0.001
Depression	108 (20.19)	77 (17.42)	75 (16.13)	0.231
Physical activity, h/week	2.92 (1.04, 5.17)	2.75 (1.00, 4.67)	2.33 (0.75, 4.33)	0.037
Social activity	2.80 (2.33, 3.00)	2.67 (2.20, 3.00)	2.50 (2.17, 3.00)	<0.001

Values are mean ± SD, n (%), or median (interquartile range).

*FGCRS categories: lowest group (4 to 13); middle group (14 to 16); highest group (17 to 28).

Abbreviations: BMI, Body mass index; HDL-C, High-density lipoprotein cholesterol; SBP, Systolic blood pressure; TC, Total cholesterol; FVC, Forced vital capacity; FEV1, Forced expiratory volume in one second; PEF, Peak expiratory flow.

Missing data: BMI = 25; Stroke = 112; Congestive heart failure = 77; Heart diseases = 1.

indicated that hypertension, diabetes, and dyslipidemia are not associated with FEV1, FVC, or PEF decline [11, 16]. In these studies, PF was assessed using a single PF index without considering the use of a comprehensive combination of FEV1, FVC, and PEF to reflect the function of some respiratory muscles [17]. Given that cardiovascular risk factors often interact with each other, in the present study, FGCRS, as a comprehensive indicator, was used to assess multiple cardiovascular risk factors. However, the relationship between comprehensive cardiovascular risk indicators and PF decline has not yet been studied. In the present study, we found that higher FGCRS-assessed cardiovascular risk burden was related to faster PF decline (including FEV1 and FVC), especially among people with CVD. However, higher FGCRS was not significantly related to faster decline in PEF.

Several studies have shown that low physical and social activities are related to faster decline in PF [14, 18]. Therefore, assessing the role of physical and social activity in the association of cardiovascular burden with PF decline is needed for the primary prevention of pulmonary dysfunction. However, only two studies have explored the joint effects of physical and social activities with individual cardiovascular factors on PF decline. A cohort study showed that moderate-high levels of regular physical activities are related to a reduction in smoking-related PF decline [14]. Another longitudinal study demonstrated that active social activity might contribute to less age-related decline in

Table 2. Association of the Framingham general cardiovascular risk score (FGCRS) with the changes of pulmonary function.

FGCRS	Pulmonary function	FEV1	FVC	PEF
	β (95% CI)*	β (95% CI)*	β (95% CI)*	β (95% CI)*
Baseline				
Continuous FGCRS	-0.017† (-0.027 to -0.006)	-0.009† (-0.016 to -0.003)	-0.010† (-0.017 to -0.002)	-0.018† (-0.030 to -0.006)
Categories FGCRS				
Lowest	Reference	Reference	Reference	Reference
Middle	-0.026 (-0.117 to 0.065)	-0.010 (-0.067 to 0.047)	-0.010 (-0.073 to 0.054)	-0.041 (-0.144 to 0.061)
Highest	-0.094† (-0.188 to -0.001)	-0.045 (-0.104 to 0.014)	-0.050 (-0.115 to 0.015)	-0.120† (-0.226 to -0.015)
Longitudinal				
Continuous FGCRS × time	-0.002† (-0.003 to -0.000)	-0.001† (-0.002 to -0.000)	-0.001† (-0.002 to -0.000)	-0.001 (-0.002 to 0.000)
Categories FGCRS × time				
Lowest	Reference	Reference	Reference	Reference
Middle	-0.010† (-0.020 to -0.001)	-0.005 (-0.011 to 0.001)	-0.008† (-0.014 to -0.001)	-0.008 (-0.021 to 0.004)
Highest	-0.013† (-0.023 to -0.003)	-0.008† (-0.014 to -0.002)	-0.009† (-0.016 to -0.002)	-0.009 (-0.021 to 0.004)

*Model adjusted for sex, age, education, body mass index, alcohol consumption, physical activity, social activity, depression, stroke, congestive heart failure, and heart diseases.

†$P < 0.05$.

Abbreviations: FVC, Forced vital capacity; FEV1, Forced expiratory volume in one second; PEF, Peak expiratory flow.

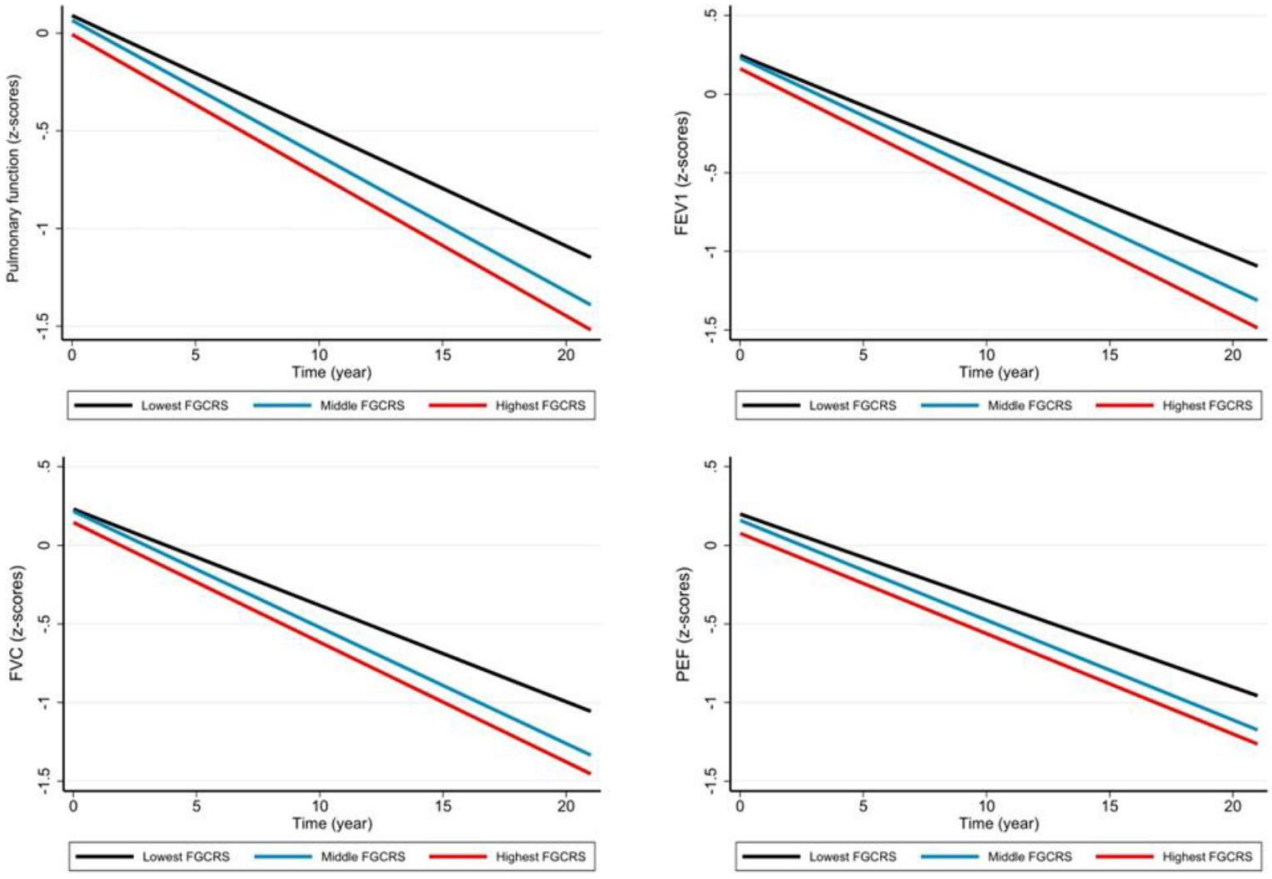

Figure 1. Pulmonary function trajectories and different domains by Framingham general cardiovascular risk score (FGCRS) tertiled. Note: Trajectories represent β-coefficients from linear mixed-effect models adjusted for sex, age, education, body mass index, alcohol consumption, physical activity, social activity, depression, stroke, congestive heart failure, and heart disease, with the lowest FGCRS group as reference group. Abbreviations: FVC, Forced vital capacity; FEVl, Forced expiratory volume in one second; PEF, Peak expiratory flow.

Table 3. Joint effects of high Framingham general cardiovascular risk score (FGCRS) with cardiovascular disease (CVD), physical activity and social activity in relation to the decline on pulmonary function.

Joint exposure		No. of subjects	Pulmonary function β (95% CI)*
FGCRS	**Physical activity**		
Low	High	279	Reference
	Low	256	-0.005 (-0.018 to 0.008)
High	High	443	-0.010 (-0.021 to 0.001)
	Low	464	-0.014† (-0.026 to -0.003)
	P-interaction= 0.048		
FGCRS	**Social activity**		
Low	High	269	Reference
	Low	266	-0.006 (-0.018 to 0.007)
High	High	377	-0.006 (-0.017 to 0.005)
	Low	530	-0.020† (-0.031 to -0.009)
	P-interaction= 0.016		
FGCRS	**CVD**		
Low	No	462	Reference
	Yes	73	0.002 (-0.017 to 0.020)
High	No	710	-0.008† (-0.016 to -0.000)
	Yes	197	-0.023† (-0.034 to -0.011)
	P-interaction= 0.017		

*Model adjusted for sex, age, education, body mass index, alcohol consumption, depression, as well as physical activity, social activity, and CVD, if applicable.
†$P < 0.05$.

PF [18]. Furthermore, FGCRS was used to assess an individual's risk of developing CVD, while specific investigations on the association of FGCRS with PF decline among CVD populations are scarce. In the current study, we found that higher FGCRS-assessed cardiovascular risk burden was related to faster decline in PF, especially among people with CVD. In addition, high levels of physical and social activities significantly mitigate the PF decline related to higher FGCRS. Our findings suggest that engagement in physical and social activities could be encouraged as a prevention strategy to delay PF decline in elderly people. We failed to find a significant interaction between FGCRS and smoking on PF. There are several explanations. First, in this study, smoking status was used as a dichotomized variable, instead of precise assessment such as cumulative tobacco consumption. Second, the sample size is limited for the examination of interactions between FGCRS and smoking on PF decline. Because the MAP study participants were healthier than the general elderly population and the prevalence of smoking was lower than in other populations. Finally, smoking is associated with elevated mortality, thus those who had heavy smoking could not be survived till old age, as a result, those who were included in the study could have less or light smoking. Thus, further large cohort studies are needed to elucidate the role of smoking in the association between FGCRS and PF.

Several mechanisms may underlie the association of cardiovascular risk burden with PF decline. First, several cardiovascular risk factors (increasing age, insulin resistance, etc.) may contribute to decreased static elastic retraction of the lung or fat deposition between the muscles and ribs, leading to the decrease of chest wall compliance and respiratory muscle strength [19, 20], thereby PF decreasing. Second, smoking, hypertension, and dyslipidemia may induce systemic inflammation and accumulation of inflammatory cells into the airways, resulting in airway structure remodeling and the destruction of the lung parenchyma, which in turn leads to a decreased PF [21, 22]. Third, regular physical activity may suppress the production of inflammatory factors, reduce airway inflammatory damage and lung parenchymal destruction, and delay the decline in lung function induced by cardiovascular risk factors through inflammation [14, 22, 23]. In addition, a high level of physical activity may reduce sedentary-induced obesity, thereby avoiding pulmonary

mechanical damage caused by additional loading of the rib cage by adipose tissue, which delays the decline in lung function induced by cardiovascular factors [24–26]. Finally, active social activities may directly improve overall health by increasing positive emotions, and therefore slow down the decline in PF [27, 28].

There are several strengths in this study. Firstly, our study is a population-based cohort study with a larger sample size and longer follow-up examination, which enables to capture trajectories of PF annually. In addition, this study assessed the comprehensive cardiovascular risk burden and an aggregated indicator of PF. However, some limitations also exist. Firstly, the participants in this study were volunteers who were more well-educated than the general population, which might contribute to limitations in the generalizability of the results. Secondly, the information on CVD and depression were according to self-report, which may lead to misclassification. Thirdly, even if FGCRS was assessed at baseline, reverse causal may exist in the relationship of PF with FGCRS. However, we repeated the analysis by excluding subjects with COPD at baseline, and the correlation remained significant. Finally, potential confounding due to residual confounders (such as dietary factors [29], working environment [30], and air pollutants [31]) could not be entirely ruled out.

Conclusively, this study proves that higher FGCRS is related to a faster PF decline, especially among people with CVD. There were significant interactions between higher FGCRS and physical/social activity, and adequate physical and social activities may mitigate PF decline related to a higher cardiovascular risk burden.

MATERIALS AND METHODS

Study population

The MAP is an ongoing prospective cohort study of common chronic conditions in older adults [32]. Briefly, older adults without known dementia were recruited from retirement communities, senior and subsidized housing, church groups, and social service agencies in northeastern Illinois, Chicago, USA (https://www.radc.rush.edu/) [33].

From 1997, 2,192 participants were enrolled and annually followed for up to 22 years till 2020 [17]. Among them, 750 participants with missing baseline FGCRS (n=417), chronic obstructive pulmonary disease (COPD) cases (n=99), or lacking follow-up PF information (n=526) were excluded, and 1,442 individuals were enrolled in the current analysis (Figure 2).

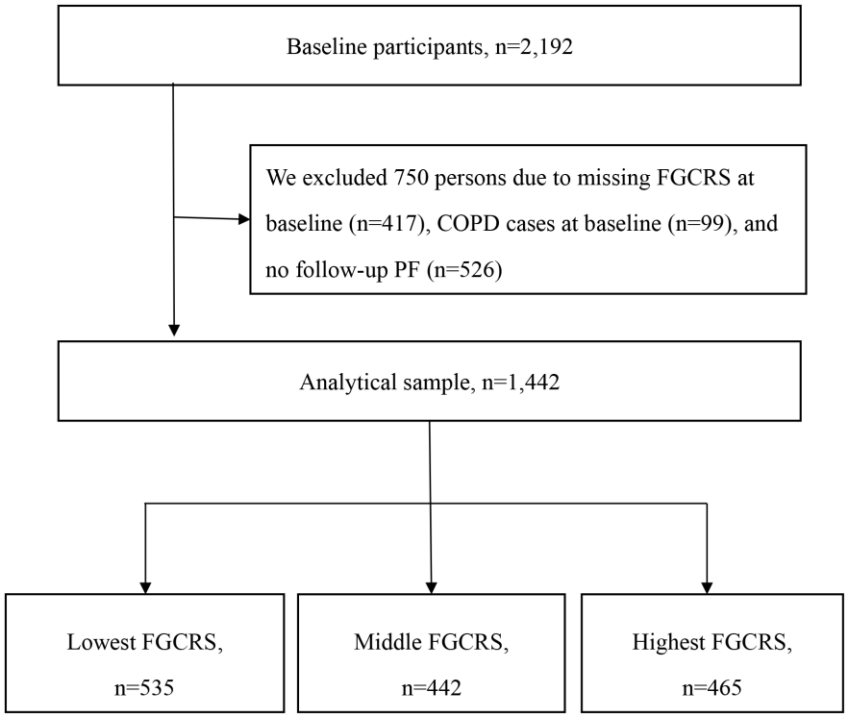

Figure 2. Flow chart of the study population. Abbreviation: FGCRS, Framingham General Cardiovascular Risk Score; COPD, chronic obstructive pulmonary disease; PF, pulmonary function.

MAP was approved by an Institutional Review Board of Rush University Medical Center. Written informed consent was obtained from all participants as well as a repository consent to allow their data to be shared.

Data collection

A comprehensive clinical assessment was conducted at baseline, and information on demographics, lifestyle factors, and the histories of diseases was collected [32]. Education was represented as the years of formal school. Body mass index (BMI) was calculated by weight (kg) /height (m^2). Smoking status was classified as never, former, or current smoker. Alcohol consumption was measured by the average amount of alcohol (grams) consumed per day over the previous year [34].

Physical activity was collected by the total weekly participation hours in walking, garden work, calisthenics, riding, and swimming [35, 36]. Social activity was rated to involve common types of social activities during the previous year. These item scores yielded the composite measurement, with higher scores reflecting more engagement in social activities [37, 38]. Both physical activity and social activity were classified as low vs. high levels by the median.

Blood pressure in the left arm was measured with a regularly tested mercury sphygmomanometer after a 5-minute interval following a standard protocol while participants were seated in a quiet room [39]. The average of the two readings was used. Hypertension was ascertained based on SBP ≥140 mm Hg, DBP ≥ 90 mm Hg, or usage of antihypertensive medication [40]. Diabetes was ascertained by HbA1c ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dl, random blood glucose ≥ 200 mg/dl, diabetes diagnosis, or usage of anti-diabetic drugs [41]. Depression was identified by the doctor or the usage of antidepressants. CVD includes stroke, congestive heart failure, and heart diseases.

Assessment of FGCRS

Baseline FGCRS was calculated by age, sex, smoking, total cholesterol, high-density lipoprotein cholesterol (HDL-C), SBP, anti-hypertension drugs, and diabetes based on the Framingham prediction model (Supplementary Tables 1, 2) [12]. FGCRS is calculated by adding the scores for all these risk factors and further dividing them into tertiles (i.e., lowest, middle, and highest). A higher FGCRS score indicates a greater risk of developing cardiovascular disease.

Assessment of PF

PF, including FVC, FEV1, and PEF, was measured twice by a hand-held spirometer (MicroPlus Spirometer MS03, MicroMedical LTC. Kent, UK) [42, 43]. The average of the two measures was used for each subject. Raw scores of the averaged measurements (i.e., FVC, FEV1, and PEF) were transformed into z-scores. Moreover, a composite PF score was calculated by averaging the z-scores of FVC, FEV1, and PEF, respectively as previously reported [17]. Possible COPD was ascertained by FEV1 / FVC≤ 0.7 [17].

Statistical analysis

Differences in characteristics among FGCRS categories of the study population were compared by one-way analysis of variance or Wilcoxon rank-sum tests for continuous variables, and chi-square tests for categorical variables.

The associations of FGCRS (as continuous and categorical variables) with changes in PF including PEF, FEV1, and FVC were analyzed using linear mixed-effects models and the β-coefficients and 95% confidence intervals (CIs) were estimated. The fixed effect included FGCRS, time (year), and their interaction, as well as all covariates. The random effect included random intercept and slope, allowing the individual differences at baseline and across time. Age, sex, education, BMI, alcohol consumption, physical activity, social activity, depression, stroke, congestive heart failure, and heart diseases were considered as confounders. The combined effect of two factors was assessed by creating dummy variables based on joint exposures of FGCRS and CVD, physical activity, social activity, and smoking status. Statistical interaction was tested by including the physical/social/CVD/ smoking status, FGCRS, time, and their cross-product index in the model.

In sensitivity analysis, we performed the analyses by excluding PF observations at baseline and within the first 2 years during the follow-up. *P*-values< 0.05 were considered statistically significant. All statistical analyses were performed using Stata SE 16.0 for Windows (StataCorp, College Station, TX, USA).

Abbreviations

BMI: Body mass index; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CVD: Cardiovascular disease; FEV1: Forced expiratory volume in one second; FGCRS: Framingham General Cardiovascular Risk Score; FVC: Forced vital capacity; HDL-C: High-density lipoprotein cholesterol; PEF: Peak expiratory flow; PF: Pulmonary function; SBP: Systolic blood pressure; TC: Total cholesterol.

AUTHOR CONTRIBUTIONS

All the authors were involved in the study concept, interpreted the data. BY and WJ were involved in manuscript writing. WJ analysed the data. Bennett and Xu supervised this study project. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to the participants and staff involved in data collection and management in the Rush Memory and Aging Project.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

ETHICAL STATEMENT AND CONSENT

Memory and Aging Project (MAP) was approved by an Institutional Review Board of Rush University Medical Center, Chicago, IL, USA. Written informed consent was obtained from all participants as well as a repository consent to allow their data to be shared.

FUNDING

Weili Xu received grants from the Swedish Research Council (No. 2017-00981 and No. 2021-01647), the Swedish Council for Health Working Life and Welfare (2021-01826), Karolinska Institutet Research Foundation (2020-01660), the Lindhés Advokatbyrå AB (2021-0134), and Stiftelsen för Gamla Tjänarinnor (2021-2022). David Bennett received grants from the National Institutes of Health (R01AG17917 and UH2NS100599).

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SUPPLEMENTARY MATERIALS

Supplementary Tables

Supplementary Table 1. Framingham general cardiovascular risk score (FGCRS) calculating for women.

Points	Age (years)	HDL-C (mg/dl)	TC (mg/dl)	SBP not treated (mm Hg)	SBP treated (mm Hg)	Smoker	Diabetic	
-3				<120				
-2		60+						
-1		50-59			<120			
0	30-34	45-49	<160	120-129		No	No	
1		35-44	160-199	130-139				
2	35-39	<35		140-149	120-129			
3			200-239		130-139	Yes		
4	40-44		240-279	150-159			Yes	
5	45-49		280+	160+	140-149			
6					150-159			
7	50-54				160+			
8	55-59							
9	60-64							
10	65-69							
11	70-74							
12	75+							
Points allotted								Total

Abbreviations: HDL-C, High-density lipoprotein cholesterol, SBP, Systolic blood pressure, TC, Total cholesterol.

Supplementary Table 2. Framingham general cardiovascular risk score (FGCRS) calculating for men.

Points	Age (years)	HDL-C (mg/dl)	TC (mg/dl)	SBP not treated (mm Hg)	SBP treated (mm Hg)	Smoker	Diabetic	
-2		60+		<120				
-1		50-59						
0	30-34	45-49	<160	120-129	<120	No	No	
1		35-44	160-199	130-139				
2	35-39	<35	200-239	140-159	120-129			
3			240-279	160+	130-139		Yes	
4			280+		140-159	Yes		
5	40-44				160+			
6	45-49							
7								
8	50-54							
9								
10	55-59							
11	60-64							
12	65-69							
13								
14	70-74							
15	75+							
Points allotted								Total

Abbreviations: HDL-C, High-density lipoprotein cholesterol, SBP, Systolic blood pressure, TC, Total cholesterol.

Supplementary Table 3. Association of the covariates with the changes of pulmonary function.

Variables	Pulmonary function	FEV1	FVC	PEF
	β (95% CI)*	β (95% CI)*	β (95% CI)*	β (95% CI)*
Age	-0.49 (-0.57, -0.42)†	-0.54 (-0.63, -0.46)†	-0.52 (-0.60, -0.44)†	-0.50 (-0.56, -0.40)†
Sex	1.15 (1.07, 1.24)†	1.20 (1.10, 1.30)†	1.22 (1.12, 1.31)†	1.15 (1.05, 1.24)†
Education	0.02 (0.01, 0.03)†	0.02 (0.00, 0.03)†	0.02 (0.01, 0.03)†	0.03 (0.02, 0.04)†
Body mass index	-0.01 (-0.01, 0.00)	-0.01 (-0.02, 0.00)	-0.01 (-0.02, 0.00)	0.00 (-0.01, 0.01)
Alcohol consumption	0.00 (-0.01, 0.01)	0.00 (-0.01,0.01)	0.00 (-0.01,0.01)	0.00 (-0.00, 0.00)
Physical activity	0.17 (0.10, 0.24)†	0.19 (0.11, 0.27)†	0.19 (0.11, 0.27)†	0.15 (0.07, 0.23)†
Social activity	0.10 (0.03, 0.17)†	0.10 (0.02, 0.19)†	0.07 (-0.01, 0.15)	0.14 (0.06, 0.22)†
Depression	-0.06 (-0.15, 0.03)	-0.06 (-0.16, 0.05)	-0.02 (-0.13, 0.08)	-0.11 (-0.21, -0.01)†
Stroke	-0.10 (-0.23, 0.03)	-0.09 (-0.23, 0.06)	-0.10 (-0.24, 0.04)	-0.13 (-0.27, 0.01)
Congestive heart failure	-0.33 (-0.50, -0.15)†	-0.40 (-0.59, -0.20)†	-0.38 (-0.58, -0.19)†	-0.22 (-0.42, -0.03)†
Heart diseases	-0.08 (-0.20, 0.04)	-0.10 (-0.24, 0.04)	-0.04 (-0.18, 0.10)	-0.11 (-0.25, 0.03)

*Model adjusted for sex, age, education, body mass index, alcohol consumption, physical activity, social activity, depression, stroke, congestive heart failure, and heart diseases.
P < 0.05.
Abbreviations: FVC, Forced vital capacity; FEV1, Forced expiratory volume in one second; PEF, Peak expiratory flow.

Supplementary Table 4. Joint effect of high Framingham general cardiovascular risk score (FGCRS) and smoking status in relation to the decline on pulmonary function.

Joint exposure		No. of subjects	Pulmonary function[a]
			β (95% CI)
FGCRS	**Smoking status**		
Low	Non-smokers	308	Reference
Low	Smokers[b]	227	-0.009 (-0.022 to 0.004)
High	Non-smokers	550	-0.016[c] (-0.027 to -0.006)
High	Smokers[b]	357	-0.015[c] (-0.026 to -0.004)

[a]Model adjusted for sex, age, education, body mass index, alcohol consumption, depression, physical activity, social activity, and CVD.
P-interaction > 0.05.
[b]Smokers including former and current smokers.
Abbreviation: CI, confidence interval.
[c]*P* < 0.05.

Supplementary Table 5. Association of the Framingham general cardiovascular risk score (FGCRS) with the changes of pulmonary function after excluding pulmonary function at baseline and within first 2 year during the follow-up (N=1,007).

FGCRS	Pulmonary function	FEV1	FVC	PEF
	β (95% CI)[a]	β (95% CI)[a]	β (95% CI)[a]	β (95% CI)[a]
Baseline				
Continuous FGCRS	-0.018[b] (-0.030 to -0.006)	-0.019[b] (-0.035 to -0.003)	-0.018[b] (-0.017 to -0.002)	-0.022[b] (-0.039 to -0.005)
Categories FGCRS				
Lowest	Reference	Reference	Reference	Reference
Middle	-0.014 (-0.131 to 0.102)	-0.003 (-0.137 to 0.132)	-0.007 (-0.143 to 0.130)	-0.014 (-0.159 to 0.131)
Highest	-0.081 (-0.204 to 0.041)	-0.072 (-0.213 to 0.068)	-0.070 (-0.212 to 0.073)	-0.132 (-0.282 to 0.018)
Longitudinal				
Continuous FGCRS × time	-0.001[b] (-0.002 to -0.000)	-0.001[b] (-0.003 to -0.000)	-0.001[b] (-0.003 to -0.000)	-0.001 (-0.003 to 0.000)
Categories FGCRS × time				
Lowest	Reference	Reference	Reference	Reference
Middle	-0.011[b] (-0.020 to -0.002)	-0.010 (-0.021 to 0.000)	-0.011 (-0.023 to 0.001)	-0.014 (-0.031 to 0.004)
Highest	-0.013[b] (-0.023 to -0.004)	-0.015[b] (-0.025 to -0.004)	-0.013[b] (-0.025 to -0.001)	-0.010 (-0.028 to 0.007)

[a]Model adjusted for sex, age, education, body mass index, alcohol consumption, physical activity, social activity, depression, stroke, congestive heart failure, and heart diseases.
[b]$P < 0.05$.