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SLEEP

# Impact of Lung Function and SDB on Incident Myocardial Infarction and Heart Failure: A Community-based Study

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## Abstract

**Purpose** To investigate whether lung function, especially when complicated with SDB, has an increased risk for myocardial infarction (MI) and congestive heart failure (CHF).

**Methods** A prospective study was performed within the Sleep Heart Health Study (SHHS). A total of 4161 individuals were followed up for an average of 10.91 years. Forced vital capacity (FVC), forced expiratory volume in one second ($FEV_1$) and the predicted value of FVC and $FEV_1$ were measured to evaluate lung function. The primary outcomes were the MI and CHF. Cox regression analysis was used to investigate the association between reduced lung function and the incidence of MI or CHF. In subgroup analysis, all the individuals were divided into Apnoea–Hypopnoea Index (AHI) < 5 subgroup and AHI ≥ 5 subgroup to explore the relationship.

**Results** Lung function were inversely associated with the incidence of MI or CHF. The hazard ratio (HR) and 95% confidence interval (95% CI) for MI and CHF were 0.658 (0.543–0.797) and 0.792 (0.673–0.933) for every 1 L increase in FVC, 0.715 (0.567–0.902) and 0.738 (0.605–0.900) for every 1 L increase in $FEV_1$, 0.986 (0.979–0.993) and 0.989 (0.983–0.995) for every 1% increase in $FEV_1$/pre%, and 0.994 (0.988–0.999) and 0.991 (0.987–0.996) in FVC/pre%, respectively. In addition, the association of lung function with MI and CHF was more prominent in the subgroup with AHI ≥ 5.

**Conclusions** Lung function may be associated with incident MI and CHF in this large community cohort of middle-aged and older adults, especially in those with SDB.

**Keywords** Lung function · Myocardial infarction · Congestive heart failure · Sleep-disordered breathing · Risk factor

## Introduction

Chronic obstructive pulmonary disease (COPD) associated with progressive airflow limitation has been documented in a close relationship with cardiovascular diseases [1]. According to the new international guideline, the diagnosis and classification of COPD almost entirely depend on lung function measurements, including forced vital capacity (FVC) and forced expiratory volume in 1 second ($FEV_1$) [2]. Because patients with lung function impairments are prone to poor sleep quality, in addition to disturbances in ventilation and gas exchange during sleep, sleep-disordered breathing (SDB) is also very common in these patients [3]. The overlap of COPD and SDB, called overlap syndrome, is also reportedly associated with increased hospitalization and all-cause mortality [4].

FVC is the maximum amount of air a person can expel from the lungs after a maximum inhalation and $FEV_1$ is the volume of air that can be forcibly blown out in the first second. Both of them are important and common in health examination, and a significant proportion of the population were found to have mild abnormal lung function, though the values did not reach those of the COPD diagnostic criteria [5]. Previously, Putcha and co-workers reported a notable association between reduced lung function and higher risk of mortality in individuals without serious SDB [6]. In addition, our published study has found that community-based

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population with reduced lung function had higher risk of stroke [7]. However, whether reduced lung function, especially in patients with SDB, has an increased risk for myocardial infarction (MI) or congestive heart failure (CHF) is still unknown. Thus, this study aimed to investigate the association between reduced lung function and the incidence of MI or CHF in a geographically diverse, community-based population with or without SDB in the SHHS cohort.

## Methods

### Study Design

The SHHS is a community-based, prospective cohort study of the cardiovascular consequences of SDB (ClinicalTrials.gov Identifier: NCT00005275) [8]. Briefly, adults 40 years of age and older were recruited from participants in existing population-based studies of cardiovascular diseases (the "parent cohorts"). Of 10737 parent cohort participants invited to participate in the SHHS, 5804 (54.05%) were enrolled in the study with informed consent and a completed acceptable polysomnogram [9]. Incident MI or CHF, the primary endpoint for this report, was defined as the first occurrence of MI or CHF without any history of MI, CHF, stroke, or revascularization procedures between the baseline polysomnogram and the final follow-up date of December 07, 2011. The individuals were followed up for an average of 10.91 years. Ongoing surveillance for incident MI events was performed by the parent cohorts according to cohort-specific protocols [10, 11]. The protocol was approved by the Institutional Review Board of each participating institution (Boston University, Case Western Reserve University, Johns Hopkins University, Missouri Breaks Research, Inc., New York University Medical Center, University of Arizona, University of California at Davis, University of Minnesota—Clinical and Translational Science Institute, University of Washington). The data were accessed based on signed agreement with the Brigham and Women's Hospital.

### Lung Function and SDB

Participants in the SHHS underwent in-home polysomnography with the Compumedics P-series portable monitor (Abbotsford, Victoria, Australia). The polysomnograms were scored centrally as described elsewhere [12]. Apnoea was identified by a clearly discernible decrease in airflow or chest or abdominal plethysmograph amplitude that lasted for at least 10 s; both Apnoeas and hypopnoeas required an associated 4% or greater oxyhaemoglobin desaturation. The Apnoea-Hypopnoea Index (AHI) was defined as the average number of Apnoeas plus hypopnoeas per hour of sleep. Lung function, including FVC, $FEV_1$, the percentage of FEV1 as its predicted value (FVC/pre%), and the percentage of FVC as its predicted value ($FEV_1$/pre%) was measured using spirometry as per the American Thoracic Society criteria [13]. The predicted values of FVC and FEV1 was calculated according for each individual's age (in years) and height (in metres) using the following equations [14]:

$$\text{Women: predicted FVC} = 3.54 + 4.53 \times (\text{Height} - 1.65) - 0.024 \times (\text{Age} - 45)$$
$$\text{predicted FEVI} = 2.72 + 3.50 \times (\text{Height} - 1.65) - 0.025 \times (\text{Age} - 45)$$

$$\text{Men: predicted FVC} = 4.84 + 5.83 \times (\text{Height} - 1.75) - 0.032 \times (\text{Age} - 45)$$
$$\text{predicted FEVI} = 3.63 + 3.62 \times (\text{Height} - 1.75) - 0.032 \times (\text{Age} - 45)$$

### Other Covariates

During the SHHS home visit, before the polysomnogram, a study technician collected the health history using a standardised questionnaire. Smoking status was classified as "never" (if the participant reported lifetime smoking of fewer than 20 packs of cigarettes), former, or current. Blood pressure measurements were obtained using a standardised protocol at the SHHS baseline examination [8]. History of hypertension was identified based on second and third blood pressure readings or being treated with hypertension medication. History of diabetes was ascertained based on report of physician diagnosis or reported use of insulin or oralhypoglycaemic medication.

### Statistical Analysis

Participants were followed until a first MI or CHF occurred between the date of the polysomnogram and the final censoring date. Descriptive statistics are presented by category of FVC or $FEV_1$ quartiles. We used analysis of variance (ANOVA) for continuous variables and the Chi square test for categorical variables. Values represent mean ± standard deviation or number (percentage). A general linear model was used to show the association between lung function and other covariates. The primary analyses used Cox proportional hazards regression modeling to examine the association of baseline lung function with incident MI or CHF outcomes. Specifically, covariates from the baseline SHHS examination included in the adjusted models were: (1) age, sex; (2) these variables plus body mass index (BMI), smoking status, total cholesterol, high-density lipoprotein, and triglyceride levels, which may serve as risk factors for MI or CHF; (3) these variables plus AHI, history of diabetes, and history of hypertension. Survival curves were also conducted to represent the difference of two outcomes between subjects with different AHI and lung function. Subgroup analysis was further used to investigate the correlation of lung function with MI and CHF stratified by AHI level (AHI < 5 and AHI ≥ 5). All analyses were performed using SPSS 24.0 (SPSS Inc., Xi'an Jiaotong University, China). A two-sided $p$ value < 0.05 was considered statistically significant.

## Results

Of the 5804 subjects enrolled in the SHHS, 600 were excluded because of prevalent MI, CHF, stroke, or revascularisation procedures at baseline. In addition, excluded were an additional 762 subjects without follow-up data and

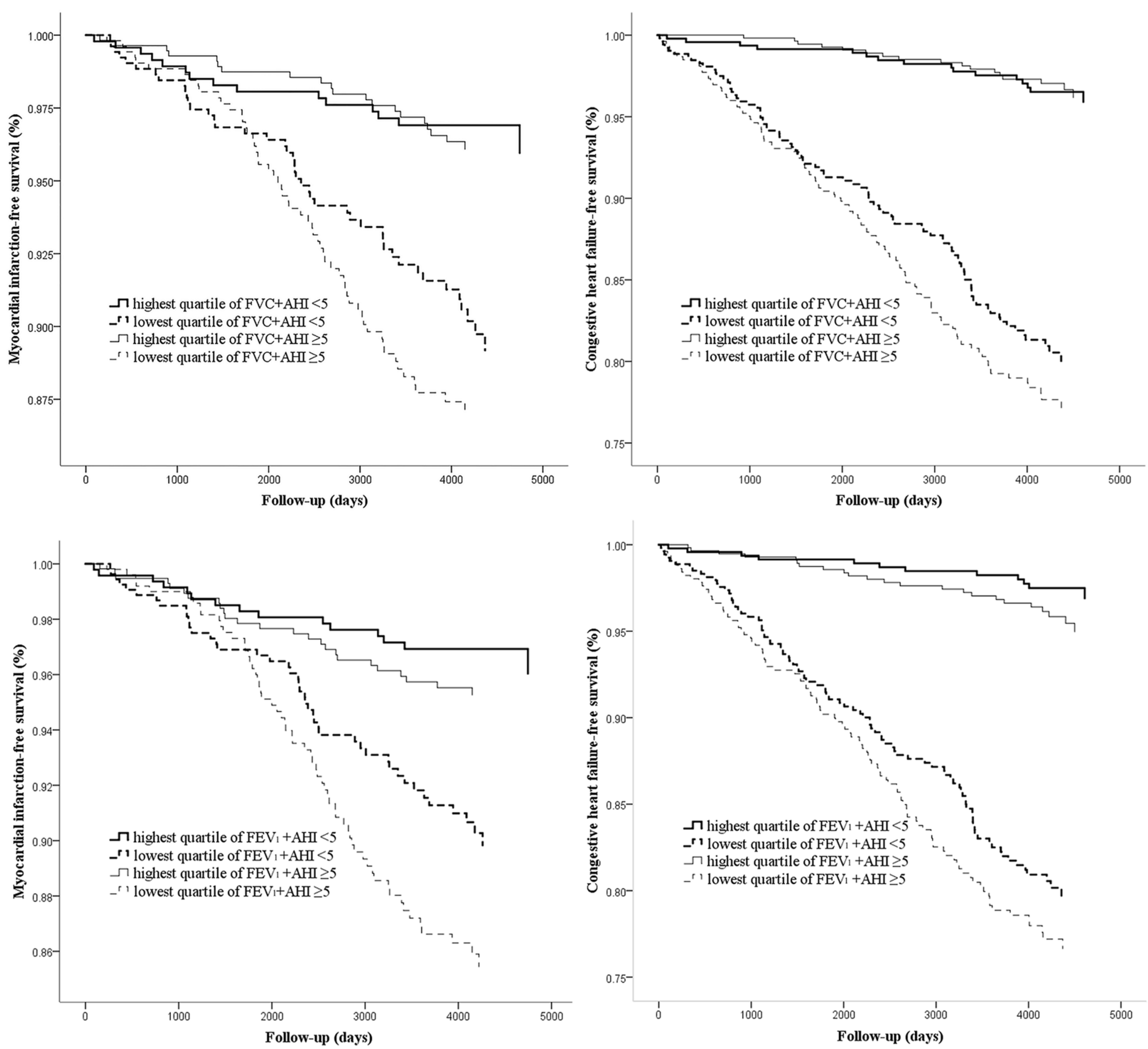


**Fig. 1** Unadjusted survival curves for incident MI or CHF by different lung function and AHI. *MI* myocardial infarction, *CHF* congestive heart failure, *FVC* forced vital capacity, $FEV_1$ forced expiratory volume in one second, *AHI* Apnoea-Hypopnoea index

43 subjects who were missing baseline FVC and $FEV_1$, which allowed 4161 subjects for the present analysis (Supplementary Fig. 1). Eventually, 1848 men and 2313 women were followed up for an average of 10.91 years (maximum: 15.87). The mean FVC was 3.53 L (± 1.03 L) in the AHI < 5 group and 3.61 L (± 1.06 L) in the AHI ≥ 5 group, while the mean $FEV_1$ was 2.66 L (± 0.80 L) and 2.72 L (± 0.81 L), respectively.

As expected, decreasing FVC or $FEV_1$ was associated with older age, higher BMI, higher cholesterol and triglyceride levels, and higher prevalence of hypertension and diabetes. Moreover, female sex, non-smoker status, and higher high-density lipoprotein levels were noted in the low FVC and $FEV_1$ quartile group (Tables 1, 2). As two commonly used variables reflecting lung function, there was a significant linear association between FVC and $FEV_1$ ($r = 0.948$, $p < 0.001$).

During the follow-up period, 256 cases of MI and 402 of CHF were identified in this incident cohort, including 106 cases of MI and 150 of CHF in the AHI < 5 subgroup and 150 cases of MI and 242 of CHF in the AHI ≥ 5 subgroup. There was a significant inverse association between lung function and incidence of MI or CHF. Even after adjustment for multiple variables, the risk of MI significantly decreased

**Table 1** Characteristics of subjects by quartiles of FVC

| | Quartiles of FVC | | | | *p* for trend |
|---|---|---|---|---|---|
| | Q1 (low) | Q2 | Q3 | Q4 (high) | |
| FVC range (L) | < 2.83 | 2.83–3.48 | 3.49–4.25 | ≥ 4.26 | |
| Subjects (*n*) | 1056 | 1039 | 1027 | 1039 | |
| Age (years) | 71.60 ± 9.96 | 62.92 ± 10.29 | 60.99 ± 9.72 | 58.05 ± 8.70 | < 0.001 |
| BMI (kg/m$^2$) | 28.39 ± 5.34 | 28.33 ± 5.42 | 28.20 ± 5.06 | 28.14 ± 4.11 | 0.206 |
| Sex [*n* (%)] | | | | | |
| Male | 136 (12.87) | 241 (23.19) | 509 (49.56) | 962 (92.58) | < 0.001 |
| Female | 920 (87.12) | 798 (76.90) | 518 (50.43) | 77 (7.41) | |
| Race [*n* (%)] | | | | | |
| White | 844 (79.92) | 899 (86.52) | 938 (91.33) | 977 (94.03) | < 0.001 |
| Black | 146 (13.82) | 56 (5.38) | 37 (3.60) | 14 (1.34) | |
| Other | 66 (6.25) | 84 (8.08) | 52 (5.06) | 48 (4.61) | |
| Smoking status [*n* (%)] | | | | | |
| Current smoker | 92 (8.71) | 96 (9.23) | 94 (9.15) | 117 (11.26) | < 0.001 |
| Ex-smoker | 391 (37.02) | 392 (37.72) | 466 (45.37) | 515 (49.56) | |
| Nonsmoker | 573 (54.26) | 551 (53.03) | 467 (45.47) | 407 (39.17) | |
| Education level [years, *n* (%)] | | | | | |
| ≤ 10 | 225 (21.30) | 178 (17.13) | 127 (12.36) | 107 (10.29) | < 0.001 |
| 11–15 | 600 (56.81) | 561 (53.39) | 504 (49.07) | 421 (40.51) | |
| 16–20 | 223 (21.11) | 275 (26.46) | 350 (34.07) | 407 (39.17) | |
| > 20 | 8 (7.57) | 25 (2.40) | 46 (4.47) | 104 (10.00) | |
| History of hypertension [*n* (%)] | 543 (51.42) | 377 (36.28) | 343 (33.39) | 243 (23.38) | < 0.001 |
| History of diabetes [*n* (%)] | 101 (9.56) | 74 (7.12) | 53 (5.16) | 40 (3.84) | < 0.001 |
| Total cholesterol (mg/dL) | 211.58 ± 41.25 | 209.55 ± 36.63 | 206.08 ± 37.12 | 201.43 ± 36.91 | < 0.001 |
| HDL (mg/dL) | 54.78 ± 15.21 | 53.44 ± 15.72 | 51.86 ± 16.99 | 45.26 ± 13.79 | < 0.001 |
| Triglyceride (mg/dL) | 156.43 ± 105.93 | 146.93 ± 83.21 | 145.37 ± 89.76 | 150.69 ± 113.75 | 0.188 |
| $FEV_1$ (L) | 1.76 ± 0.37 | 2.40 ± 0.27 | 2.90 ± 0.29 | 3.72 ± 0.50 | < 0.001 |
| FVC (L) | 2.31 ± 0.40 | 3.17 ± 0.18 | 3.84 ± 0.21 | 4.98 ± 0.56 | < 0.001 |
| AHI (events/h) | 9.83 ± 13.42 | 8.56 ± 12.08 | 10.04 ± 13.41 | 10.37 ± 12.51 | 0.086 |
| Average REM oxygen saturation (%) | 93.83 ± 2.79 | 94.60 ± 2.48 | 94.53 ± 2.31 | 94.35 ± 1.98 | < 0.001 |
| Average NREM oxygen saturation (%) | 94.30 ± 2.09 | 94.77 ± 1.91 | 94.70 ± 1.81 | 94.39 ± 1.66 | 0.446 |
| Follow-up (years) | 10.02 ± 3.26 | 10.96 ± 2.87 | 11.23 ± 2.58 | 11.44 ± 2.51 | < 0.001 |

*p* for trend values reflect a linear trend in row values from low to high FVC level. Data are presented as mean ± standard deviation or number (percentage)

*FVC* forced vital capacity, *$FEV_1$* forced expiratory volume in 1 s, *BMI* body-mass index, *HDL* high-density lipoprotein, *AHI* Apnoea-Hypopnoea Index, *REM* rapid-eye movement, *NREM*, non-rapid eye movement

**Table 2** Characteristics of subjects by quartiles of $FEV_1$

| | Quartiles of $FEV_1$ | | | | *p* for trend |
|---|---|---|---|---|---|
| | Q1 (low) | Q2 | Q3 | Q4 (high) | |
| $FEV_1$ range (L) | < 2.13 | 2.13–2.65 | 2.66–3.21 | ≥ 3.22 | |
| Subjects (*n*) | 1045 | 1049 | 1020 | 1047 | |
| Age (years) | 71.94 ± 9.30 | 63.94 ± 10.10 | 60.51 ± 9.41 | 57.28 ± 9.04 | < 0.001 |
| BMI (kg/m$^2$) | 28.06 ± 5.14 | 28.58 ± 5.39 | 28.16 ± 5.12 | 28.25 ± 4.33 | 0.817 |
| Sex [*n* (%)] | | | | | |
| Male | 163 (15.59) | 288 (27.45) | 462 (15.29) | 935 (89.30) | < 0.001 |
| Female | 882 (84.40) | 761 (72.54) | 558 (54.70) | 112 (10.69) | |
| Race [*n* (%)] | | | | | |
| White | 842 (80.57) | 911 (86.84) | 938 (91.96) | 967 (92.35) | < 0.001 |
| Black | 149 (14.25) | 60 (5.71) | 28 (2.74) | 16 (1.52) | |
| Other | 54 (5.16) | 78 (7.43) | 54 (5.29) | 64 (6.11) | |
| Smoking status [*n* (%)] | | | | | |
| Current smoker | 116 (11.10) | 88 (8.38) | 85 (8.33) | 110 (10.50) | 0.006 |
| Ex-smoker | 414 (39.61) | 411 (39.18) | 438 (42.94) | 501 (47.85) | |
| Nonsmoker | 515 (49.28) | 550 (52.43) | 497 (48.72) | 436 (41.64) | |
| Education level [years, *n* (%)] | | | | | |
| ≤ 10 | 221 (21.14) | 186 (17.73) | 114 (11.17) | 113 (10.79) | < 0.001 |
| 11–15 | 600 (57.41) | 565 (53.86) | 499 (48.92) | 425 (40.59) | |
| 16–20 | 215 (20.57) | 268 (25.54) | 362 (35.49) | 410 (39.15) | |
| > 20 | 9 (0.86) | 30 (2.85) | 45 (4.41) | 99 (9.45) | |
| History of hypertension [*n* (%)] | 530 (50.71) | 412 (39.27) | 314 (30.78) | 250 (23.87) | < 0.001 |
| History of diabetes [*n* (%)] | 98 (9.37) | 87 (8.29) | 46(4.50) | 37(3.53) | < 0.001 |
| Total cholesterol (mg/dL) | 212.19 ± 41.03 | 207.39 ± 36.40 | 208.21 ± 36.98 | 200.94 ± 37.49 | < 0.001 |
| HDL (mg/dL) | 55.13 ± 15.32 | 52.55 ± 16.05 | 52.62 ± 16.90 | 45.02 ± 13.21 | < 0.001 |
| Triglyceride (mg/dL) | 153.92 ± 103.59 | 148.38 ± 85.91 | 143.97 ± 86.36 | 153.16 ± 116.62 | 0.647 |
| $FEV_1$ (L) | 1.70 ± 0.33 | 2.38 ± 0.15 | 2.91 ± 0.15 | 3.77 ± 0.43 | < 0.001 |
| FVC (L) | 2.37 ± 0.49 | 3.19 ± 0.36 | 3.81 ± 0.37 | 4.92 ± 0.62 | < 0.001 |
| AHI (events/h) | 9.14 ± 12.51 | 9.70 ± 13.27 | 9.27 ± 12.70 | 10.66 ± 13.00 | 0.020 |
| Average REM oxygen saturation (%) | 93.83 ± 2.72 | 94.43 ± 2.59 | 94.68 ± 2.15 | 94.37 ± 2.11 | < 0.001 |
| Average NREM oxygen saturation (%) | 94.26 ± 2.01 | 94.68 ± 2.01 | 94.79 ± 1.74 | 94.43 ± 1.71 | 0.022 |
| Follow-up (years) | 9.97 ± 3.27 | 10.91 ± 2.88 | 11.32 ± 2.49 | 11.45 ± 2.54 | < 0.001 |

*p* for trend values reflect a linear trend in row values from low to high FVC level. Data are presented as mean ± standard deviation or number (percentage)

*FVC* forced vital capacity, *$FEV_1$* forced expiratory volume in 1 s, *BMI* body mass index, *HDL* high-density lipoprotein, *AHI* Apnoea-Hypopnoea index, *REM* rapid eye movement, *NREM* non-rapid eye movement

with the increase of lung function, with an HR and 95% confidence interval (95% CI) of 0.658 (0.543–0.797) for every 1 L increase in FVC and 0.715 (0.567–0.902) for every 1 L increase in $FEV_1$, respectively. Although the association between CHF and lung function was attenuated after multiple adjustments, the HR and 95% CI for CHF were 0.792 (0.673–0.933) for every 1 L increase in FVC and 0.738 (0.605–0.900) for every 1 L increase in $FEV_1$, respectively. In addition, after adjustment for multiple variables, the risk of MI and CHF significantly decreased with the increase of FVC/pre% and FEV1/pre% respectively (Table 3). Subjects in the lowest quartile of FVC or $FEV_1$ were observed to have a higher incidence of MI and CHF compared to those in the highest quartile. The highest incidences of both MI and CHF were found in the subgroup with the co-existence of the lowest quartile of lung function and AHI ≥ 5 (Fig. 1).

To further explore the potential different role of lung function on the subjects with and without SDB, cox regressions were conducted in two different AHI categories (AHI < 5, AHI ≥ 5). In unadjusted models, FVC and $FEV_1$ showed a significant inverse trend with the incidence of MI or CHF. After strict adjustment, as described above, this association between lung function and CHF was modestly diminished but remained significant in the subgroup with

**Table 3** Relation of lung function to incident MI and CHF among the whole population

| | MI | CHF |
|---|---|---|
| Number of events [*n* (%)] | 256 (6.15) | 402 (9.66) |
| FVC | | |
| Univariate | 0.636 (0.558–0.725) | 0.474 (0.424–0.529) |
| Model 1 | 0.627 (0.523–0.751) | 0.670 (0.574–0.782) |
| Model 2 | 0.632 (0.523–0.764) | 0.737 (0.626–0.867) |
| Model 3 | 0.658 (0.543–0.797) | 0.792 (0.673–0.933) |
| $FEV_1$ | | |
| Univariate | 0.563 (0.476–0.664) | 0.368 (0.319–0.423) |
| Model 1 | 0.654 (0.526–0.812) | 0.607 (0.505–0.730) |
| Model 2 | 0.680 (0.541–0.855) | 0.676 (0.556–0.823) |
| Model 3 | 0.715 (0.567–0.902) | 0.738 (0.605–0.900) |
| FVC/pre% | | |
| Univariate | 0.969 (0.963–0.976) | 0.966 (0.961–0.971) |
| Model 1 | 0.985 (0.978–0.992) | 0.984 (0.979–0.990) |
| Model 2 | 0.984 (0.977–0.991) | 0.987 (0.981–0.992) |
| Model 3 | 0.986 (0.979–0.993) | 0.989 (0.983–0.995) |
| FEV1/pre% | | |
| Univariate | 0.986 (0.980–0.992) | 0.981 (0.977–0.986) |
| Model 1 | 0.992 (0.986–0.997) | 0.988 (0.983–0.992) |
| Model 2 | 0.992 (0.986–0.998) | 0.989 (0.985–0.994) |
| Model 3 | 0.994 (0.988–0.999) | 0.991 (0.987–0.996) |

Data were presented as hazard ratios (95% confidence interval) for per 1 L decrease in FVC or $FEV_1$ and for one percentage decrease in FVC/pre% or FEV1/pre%. Model 1 adjusted for age, sex. Model 2 adjusted for age, sex, smoking status, BMI, total cholesterol, triglycerides, HDL. Model 3 adjusted for Model 2 plus AHI, history of diabetes, and history of hypertension

*MI* myocardial infarction, *CHF* congestive heart failure, *FVC* forced vital capacity, *$FEV_1$* forced expiratory volume in 1 s, *BMI* body mass index, *HDL* high-density lipoprotein, *AHI* Apnoea-Hypopnoea index

AHI ≥ 5, with an HR of 0.755 (0.611–0.932) for every 1 L increase in FVC, 0.763 (0.589–0.989) for every 1 L increase in $FEV_1$, 0.990 (0.982–0.998) for every 1% increase in FVC/pre%, and 0.994 (0.988–1.000) for every 1% increase in $FEV_1$/pre%, respectively. For MI in the subgroup with AHI ≥ 5, the HRs were 0.642 (0.499–0.825) for every 1 L increase in FVC, 0.692 (0.513–0.933) for every 1 L increase in $FEV_1$, 0.984 (0.975–0.994) for every 1% increase in FVC/pre%, and 0.992 (0.985–1.000) for every 1% increase in $FEV_1$/pre%, respectively, with little change compared to the univariate model. However, in the subgroup with AHI < 5, the association between lung function and MI and CHF was not apparent compared to AHI ≥ 5 (Table 4).

## Discussion

In this prospective, community-based cohort study, a notable association between reduced lung function and incident MI or CHF was found using cox regression. This association persisted after multiple adjustments for potential confounders and it was still a reliable risk factor for incident MI or CHF. Further, there was a consistent inverse trend between lung function and MI or CHF incidence only in the SDB subgroup. This study provided evidence that MI and CHF risks increase with the severity of lung function impairments and specifically addressed the importance of lung function measurement in community-based SDB populations.

COPD and CHF are common comorbidities, both of which represent dyspnoea as a main clinical symptom [15]. Previous studies have reported that the prevalence of CHF and MI was higher in patients with COPD than in comparison groups [16]. Unrecognised MI is also common in patients hospitalised with COPD exacerbation [17, 18]; meanwhile, COPD exacerbation was also found to increase the risk of MI during follow-up after discharge [18]. Additionally, the relation of subclinical lung function impairment with cardiovascular diseases in the absence of diagnosed pulmonary diseases has recently drawn more attention. In a cohort with long-term follow-up, low $FEV_1$ was strongly and independently associated with incident CHF [19]. Another study showed a notable association between subclinical lung function impairments and CHF even after exclusion of individuals with COPD [20]. A population-based study of middle-aged men observed the association between moderately reduced $FEV_1$ and FVC and incident heart failure hospitalization [21]. While our community-based population included relatively older subjects, lung function showed an obvious inverse association with incident CHF and MI.

A striking feature of our findings is that the association of reduced lung function and incident MI or CHF remained significant in the SDB population but not in the non-SDB population. Indeed, SDB was associated with increased risk of coronary heart disease and CHF by another report based on the SHHS [22]. The co-existence of obstructive sleep apnoea and COPD, called overlap syndrome, has also been proposed and demonstrated to lead to atrial fibrillation, pulmonary hypertension, and high mortality [23–26]. More recently, a cohort study showed a higher all-cause mortality and hospitalisation in patients with overlap syndrome [4]. In 2016, Putcha and co-workers demonstrated that both lung function and SDB were associated with all-cause mortality. However, when further analysing subgroups with moderate to severe SDB, reduced lung function was not associated with increased risk of mortality. Based on the same cohort, our study demonstrated that both $FEV_1$ and FVC were associated with the incidence of MI and CHF. Additionally, the

**Table 4** Relation of lung function to incident MI and CHF among each subgroup

| | AHI < 5 subgroup | | AHI ≥ 5 subgroup | |
|---|---|---|---|---|
| | MI | CHF | MI | CHF |
| Number of subjects (*n*) | 2088 | 2088 | 2073 | 2073 |
| Number of events [*n* (%)] | 106 (5.07) | 160 (7.66) | 150 (7.23) | 242 (11.67) |
| FVC | | | | |
| Univariate | 0.593 (0.480–0.733) | 0.434 (0.361–0.521) | 0.661 (0.560–0.780) | 0.497 (0.432–0.571) |
| Model 1 | 0.658 (0.496–0.872) | 0.727 (0.567–0.931) | 0.610 (0.481–0.773) | 0.636 (0.520–0.777) |
| Model 2 | 0.669 (0.498–0.900) | 0.807 (0.623–1.044) | 0.607 (0.474–0.779) | 0.696 (0.564–0.860) |
| Model 3 | 0.669 (0.494–0.905) | 0.845 (0.649–1.100) | 0.642 (0.499–0.825) | 0.755 (0.611–0.932) |
| $FEV_1$ | | | | |
| Univariate | 0.519 (0.398–0.676) | 0.302 (0.240–0.379) | 0.585 (0.473–0.725) | 0.409 (0.342–0.488) |
| Model 1 | 0.696 (0.495–0.980) | 0.591 (0.442–0.790) | 0.629 (0.474–0.833) | 0.618 (0.485–0.787) |
| Model 2 | 0.737 (0.513–1.058) | 0.665 (0.489–0.905) | 0.647 (0.481–0.870) | 0.690 (0.534–0.893) |
| Model 3 | 0.737 (0.509–1.066) | 0.697 (0.508–0.955) | 0.692 (0.513–0.933) | 0.763 (0.589–0.989) |
| FVC/pre% | | | | |
| Univariate | 0.972 (0.962–0.982) | 0.963 (0.955–0.971) | 0.968 (0.959–0.977) | 0.969 (0.962–0.976) |
| Model 1 | 0.986 (0.976–0.997) | 0.984 (0.976–0.992) | 0.983 (0.974–0.993) | 0.985 (0.978–0.992) |
| Model 2 | 0.987 (0.976–0.998) | 0.987 (0.978–0.995) | 0.982 (0.972–0.992) | 0.987 (0.979–0.995) |
| Model 3 | 0.987 (0.976–0.998) | 0.988 (0.979–0.997) | 0.984 (0.975–0.994) | 0.990 (0.982–0.998) |
| FEV1/pre% | | | | |
| Univariate | 0.986 (0.977–0.995) | 0.974 (0.968–0.981) | 0.985 (0.978–0.993) | 0.986 (0.980–0.992) |
| Model 1 | 0.993 (0.985–1.002) | 0.985 (0.979–0.992) | 0.991 (0.984–0.998) | 0.989 (0.984–0.995) |
| Model 2 | 0.994 (0.985–1.003) | 0.987 (0.980–0.994) | 0.991 (0.983–0.998) | 0.991 (0.985–0.997) |
| Model 3 | 0.994 (0.985–1.004) | 0.988 (0.981–0.995) | 0.992 (0.985–1.000)* | 0.994 (0.988–1.000)$^{\&}$ |

Data were presented as hazard ratios (95% confidence interval) for per 1 L decrease in FVC or $FEV_1$ and for 1% decrease in FVC/pre% or FEV1/pre%. Model 1 adjusted for age, sex. Model 2 adjusted for age, sex, smoking status, BMI, total cholesterol, triglycerides, HDL. Model 3 adjusted for Model 2 plus AHI, history of diabetes, and history of hypertension

*MI* myocardial infarction, *CHF* congestive heart failure, *FVC* forced vital capacity, $FEV_1$ forced expiratory volume in 1 s, *BMI* body mass index, *HDL* high-density lipoprotein, *AHI* Apnoea-Hypopnoea index

*$p = 0.057$; $^{\&}p = 0.044$

associations were attenuated in the normal subgroup but remained significant in the SDB subgroup. To the best of our knowledge, this is the first report showing that $FEV_1$ and FVC may be independent risk factors of MI and CHF in populations with SDB.

Several potential mechanisms to account for the observed high incident cardiovascular disease rate in subjects with lung function impairments and elevated AHI should be emphasised. First, our study indicated that the decreased level of average rapid-eye movement oxygen saturation was related to the reduced lung function at baseline. Reduced lung function and SDB may synergistically augment hypoxaemia and chronic intermittent hypoxaemia, could predispose to cardiovascular diseases by stimulating angiogenesis or promoting atherosclerosis [27]. Second, it is increasingly recognised that SDB is associated with systemic inflammation contributing to an increased risk of cardiovascular diseases [28]. The level of inflammation factors, such as TNF-α and IL-8, is elevated in patients with SDB, and is reduced with continuous positive airway pressure therapy [29]. Inflammatory response to reduced lung function is another conceivable mechanism for systematic atherosclerosis and thrombosis [30, 31]. Third, SDB is considered to lead to insulin resistance, hypertension, and cardiovascular diseases through increased sympathetic activity and oxidative stress, which may contribute to accelerate the incidence of MI or CHF in populations with reduced lung function [32, 33].

Our study had some limitations. The older age of the cohort increases the likelihood of a healthy survivor effect biasing toward a null result and precludes the assessment of cardiovascular risk in younger adults. Unmeasured cardiovascular risk factors, such as diet and exercise habits, were not taken into consideration, and confounding by these variables cannot be excluded. In addition, lung function was measured once in our study, while long-period monitoring may further help elucidate the association between lung function and cardiovascular outcomes.

## Conclusions

In conclusion, lung function may be associated with the incidence of MI and CHF in the community-based population of middle-aged and older adults. Moreover, this association remained significant in the SDB population.

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### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical Approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

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