Original Article

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Association between lung function and hypertension and home hypertension in a Japanese population: the Tohoku Medical Megabank Community-Based Cohort Study

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Background: Although several studies have shown an inverse association between lung function and hypertension, few studies have examined the association between lung function and hypertension among never-smokers, and no study has investigated the association between lung function and home hypertension. We investigated the associations between lung function and hypertension in a Japanese population.

Individuals and methods: We conducted a cross-sectional study of 3728 men and 8795 women aged 20 years or older living in Miyagi Prefecture, Japan. Lung function was assessed using forced expiratory volume at 1 s (FEV_1) and forced vital capacity (FVC), measured by spirometry. Hypertension was defined as a casual blood pressure at least 140/90 mmHg and/or self-reported treatment for hypertension. Home hypertension was defined as morning home blood pressure at least 135/85 mmHg and/or self-reported treatment for hypertension. Multivariate logistic regression models adjusted for potential confounders were used to assess the association between lung function and hypertension.

Results: The mean ages (±SD) of men and women were 60.1 (±14.0) years and 56.2 (±13.4) years, respectively, and 1994 (53.5%) men and 2992 (34.0%) women had hypertension. In the multivariable models, FEV_1 and FVC were inversely associated with hypertension. Inverse associations between lung function and hypertension were observed even among never-smokers. Furthermore, reduced lung function was associated with higher prevalence of home hypertension in men and women.

Conclusion: Reduced lung function was associated with higher prevalence of hypertension, independent of smoking status. Assessment of the lung function or blood pressure may be required in individuals with reduced lung function or hypertension.

Keywords: blood pressure, epidemiology, hypertension, lung function

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; CIs, confidence intervals; COPD, chronic obstructive pulmonary disease; CRP, C reactive protein; FEV_1, forced expiratory volume at 1s; FVC, forced vital capacity; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; METs, metabolic equivalents; ORs, odds ratios; Q, quartile; SD, standard deviation; TC, total cholesterol; TMM CommCohort Study, Tohoku Medical Megabank community-based cohort study; WBC, white blood cell

INTRODUCTION

Many prospective cohort studies have shown that reduced lung function, that is, forced expiratory volume at 1 s (FEV_1) and forced vital capacity (FVC), is associated with a higher risk of stroke, myocardial infarction, and cardiovascular mortality [1–4]. Furthermore, several studies have shown that these associations remained, even when restricted to never-smokers [1–3].

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Hypertension is a well known leading risk factor for cardiovascular disease [5]. Therefore, several studies have examined the association between lung function and hypertension [6–14], and these studies have shown that lung function is inversely associated with blood pressure (BP) and hypertension [6–13]. However, only a few studies have reported an association between lung function and hypertension among never-smokers [7,8], although smoking is closely associated with reduced lung function and is positively associated with BP [15–18]. In addition, age is closely associated not only with increased BP but also with decreased lung function because of decreased elastic recoil [10,15,19–21]. Hence, age-related confounding may have a strong impact on the association between lung function and hypertension; however, no studies have reported an association between lung function and hypertension, stratified age. Furthermore, previous studies showed that home BP is better than casual BP at predicting the onset of cardiovascular disease [22–25]. However, the association between lung function and home hypertension is unknown. Finally, to the best of our knowledge, no reports on the association between lung function and hypertension have yet been reported in a Japanese population.

Thus, we examined the cross-sectional association between lung function and the prevalence of hypertension and home hypertension in a Japanese Tohoku Medical Megabank Community-Based Cohort Study (TMM CommCohort Study) population.

METHODS

Study design and population

We conducted a cross-sectional study using data from the TMM CommCohort Study. The details have been published elsewhere [26,27]. In brief, this cohort study was aimed to contribute to the development of personalized healthcare and medicine worldwide, for which many genomic and epidemiological studies have been conducted [26–33]. To recruit participants, we used three approaches: a type 1 survey (40 433 participants) was conducted at specific municipal health check-up sites; an additional type 1 survey (664 participants) was conducted on different dates at specific municipal health check-ups; and a type 2 survey (13 855 participants) was conducted at a community support center. The same basic information was obtained through blood and urine samples, a questionnaire, and municipal health check-ups among the three approaches. Additionally, several physiological measurements (i.e. body composition and lung function tests) were performed only in type 2 survey. This study included men and women aged at least 20 years living in the Miyagi Prefecture, northeastern Japan. The survey and recruitment were conducted between May 2013 and March 2016. Informed consent was obtained from 54 952 participants. This study was approved by the Institutional Review Board of the Tohoku Medical Megabank Organization (approval number: 2022-4-047; approval date: 30 June 2022).

In this study, we only used data from type 2 survey ($n = 13\,855$) participants who underwent several physiological measurements, including lung function tests. We excluded those who withdrew from the study by 13 July 2021, failed to return the self-reported questionnaire, did not undergo physiological measurements, or had missing data regarding lung function, SBP, DBP, plasma glucose, glycated hemoglobin A1c (HbA1c), total cholesterol (TC), triglyceride, high-density lipoprotein cholesterol (HDL-C), urinary creatinine, estimated urinary 24-h sodium excretion, estimated urinary 24 h potassium excretion and white blood cell (WBC) count ($n = 1332$). Finally, data from 12 523 participants (3728 men and 8795 women) were analyzed.

Assessment of the lung function

Lung function, including FEV_1, FVC, and vital capacity (VC), was measured using a spirometer (HI-801; Chest M. I., Incorporation). The measurements were taken with the participants in a sitting position with a nose clip attached. The FEV_1 and FVC were categorized into the following sex-specific quartiles: For men, Q1 (<2.56), Q2 (2.56–2.95), Q3 (2.96–3.43), Q4 (≥3.43) in FEV_1; and Q1 (<3.28), Q2 (3.28–3.73), Q3 (3.74–4.26), Q4 (≥4.26) in FVC. For women, Q1 (<1.96), Q2 (1.96–2.25), Q3 (2.26–2.58), Q4 (≥2.58) in FEV_1; and Q1 (<2.44), Q2 (2.44–2.77), Q3 (2.78–3.14), Q4 (≥3.14) in FVC. Restrictive and obstructive ventilatory impairments were defined as reduced vital capacity of less than 80% of the predicted and reduced FVC ratio of less than 70% of FEV_1 : FVC, respectively.

Hypertension

After resting for at least 2 min in a sitting position, BP was measured twice in the upper right arm using a digital automatic BP monitor (HEM-9000AI; Omron Healthcare Co., Ltd., Kyoto, Japan) at the community support center. The mean values of the two recorded measurements were used. Hypertension was defined as SBP at least 140 mmHg, and/or DBP at least 90 mmHg, and/or self-reported treatment for hypertension. Home BP was measured using a cuff-oscillometric device (HEM-7080IC; Omron Healthcare Co., Ltd.) and was recorded for 10 days in the morning [34,35]. Home hypertension was defined as morning home SBP at least 135 mmHg, and/or home DBP at least 85 mmHg, and/or self-reported treatment for hypertension [36].

Other measurements

We used a self-reported questionnaire to assess demographic characteristics, smoking status, drinking status, education level, physical activity, and history of respiratory disease. Age was determined at the time of visit to the community support center. Smoking status was classified into four categories: never-smokers (had smoked <100 cigarettes in their lifetime), ex-smokers (had smoked ≥100 cigarettes in their lifetime and were not current smokers), current smokers (smoked ≥100 cigarettes in their lifetime and were currently smoking) [37], and unknown status. Drinking status was classified into five categories: never drinkers (had consumed little or no alcohol or were constitutionally incapable of alcohol consumption), ex drinkers (had stopped drinking alcohol), current drinker (<23 g/day), current drinker (≥23 g/day), and unknown. To calculate the amount of ethanol consumed, alcohol types were classified into six categories: sake, distilled spirits, shochu-based beverages, beer, whiskey, and wine. Alcohol intake frequency was also classified into the

following six categories: almost never, 1–3 days/month, 1–2 days/week, 3–4 days/week, 5–6 days/week, and daily. To calculate the amount of ethanol, for each type of alcohol, we multiplied the frequency of alcohol by the amount. We set the cutoff value at 23 g of ethanol, which is the traditional Japanese unit of sake [30,31,38]. Education level was classified into five categories: below high school; vocational school, junior college, or technical college; university or graduate school; other; and unknown. To calculate the amount of leisure-time physical activity (METs-min/week), the average frequency (times/week) and duration (min/time) of normal walking, brisk walking, moderate-intensity exercise, and hard-intensity exercise during leisure time were obtained using a self-reported questionnaire. Metabolic equivalents (METs) were assigned for each physical activity [39]. The value of METs-min/week was calculated by multiplying the corresponding METs, duration, and frequency. Participants answered whether they had a history of asthma, chronic bronchitis, or chronic obstructive pulmonary disease (COPD).

Height was measured to the nearest 0.1 cm using a stadiometer (AD6400; A&D Co., Ltd., Tokyo, Japan). Weight was measured in increments of 0.1 kg, and 1.0 kg was subtracted to account for the weight of the participant's clothing using a body composition analyzer (InBody720; Biospace Co., Ltd., Seoul, Korea). The BMI was calculated as weight (kg) divided by height [meters squared (m^2)].

Blood samples were collected under nonfasting conditions. Plasma glucose and HbA1c levels were measured using enzymatic methods. Diabetes was defined as plasma glucose at least 200 mg/dl, HbA1c at least 6.5%, and/or self-reported treatment for diabetes. TC was measured using an ultraviolet-end method with cholesterol dehydrogenase. The TG levels were measured using an enzymatic method. HDL-C levels were measured using a direct method. We could not calculate the low-density lipoprotein cholesterol (LDL-C) because the Friedewald formula, used to calculate LDL-C, only holds for fasting blood samples [40]. Hypercholesterolemia was defined as TC at least 240 mg/dl and/or treatment for dyslipidemia. The cut-off point was set according to the International Conference on Low Blood Cholesterol [41]. The WBC count was measured using the sheath flow electrical resistance method and sodium lauryl sulfate hemoglobin method. Casual spot urine samples from each participant were collected. Estimates of 24-h urinary excretion of sodium and potassium from the spot urine samples were calculated using the Tanaka formula [42].

Statistical analysis

Data are presented as mean [standard deviation (SD)] or median [interquartile range (IQR)] for continuous variables, and as numbers (%) for categorical variables. All analyses were performed separately for men and women because the distributions of lung function and the prevalence of hypertension differed between them.

In terms of the characteristics of the FEV_1 quartiles, a trend test was performed for continuous variables using a simple linear model to evaluate the linear association. We also conducted a chi-square test to compare the characteristics of categorical variables among the FEV_1 quartiles. We performed a similar analysis to evaluate the linear associations and compare the characteristics of the categorical variables among the FVC quartile groups.

Multivariate logistic regression analysis was used to examine the association between FEV_1 and the prevalence of hypertension. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. In model 1, we adjusted for age, height, and education level. In model 2, we further adjusted for smoking status, weight, diabetes, hypercholesterolemia, drinking status, estimated 24-h urinary excretion of sodium and potassium. Furthermore, in model 3, METs and WBC counts were included to confirm whether the association between lung function and hypertension could be explained by physical activity and inflammation. The P values for the analysis of linear trends were calculated by scoring the categories from 1 (the lowest category) to 4 (the highest category) and entering the number as a continuous term in the regression model. We also examined the association between FVC and prevalence of hypertension using the same statistical models. Furthermore, we performed an analysis with home hypertension as outcome using above same model, among participants who measured home BP more than 10 times, in order to investigate whether the inverse association between lung function and hypertension observed in casual blood pressure is also observed in home BP ($n = 2526$ for men and $n = 6119$ for women).

We conducted several sensitivity analyses. First, as smoking is strongly associated with lung function and hypertension, we stratified the analysis by smoking status (never-smoker, ex-smoker, current smoker). Second, we stratified the analysis by age (young, 20–39 years; middle-aged 40–64 years; elderly, 65–74 years; and very old, ≥75 years). Third, to rule out the effects of respiratory disease, we restricted the participants to those who had no restrictive ventilatory impairment, obstructive ventilatory impairment, or history of respiratory diseases such as asthma, chronic bronchitis, and COPD. Forth, previous studies have shown that antihypertensive drugs are associated with reduced lung function [11,43]. Hence, to rule out the influence of hypertension treatment, we selected only participants who were not undergoing treatment for hypertension.

$P < 0.05$ was considered significant. All analyses were performed using R, version 4.1.2. (R Core Team, Vienna, Austria).

RESULTS

Tables 1 and 2 presents the characteristics of the study participants. The data of 3728 men and 8795 women, who met all inclusion criteria were analyzed. The mean age (±SD) of the study participants was 60.1 years (±14.0 years) for men and 56.2 years (±13.4 years) for women. Seven hundred and fifty-four (20.2%) men and 622 (7.1%) women were current smoker. The FEV_1 and FVC were higher in men than in women. The prevalence of hypertension was also higher in men [1994 (53.5%)] than in women [2992 (34.0%)]. Among the participants, the higher the FEV_1, the lower the age, prevalence of hypertension, diabetes, and hypercholesterolemia. Moreover, participants with higher FEV_1 had higher education levels and were current smokers (Table 1). Similar patterns were observed when the FVC quartiles were used (Table 2).

TABLE 1. Participant's characteristics according to forced expiratory volume at 1 s quartile

Variables	Men	The quartile groups of FEV_1 (range)				*P* value	Women	The quartile groups of FEV_1 (range)				*P* value
		Q1 (<2.56)	Q2 (2.56-2.95)	Q3 (2.96–3.43)	Q4 (≥3.43)			Q1 (<1.96)	Q2 (1.96–2.25)	Q3 (2.26–2.58)	Q4 (≥2.58)	
Number	3728	919	934	925	950		8795	2198	2174	2166	2257	
Age (year)	60.1 (14.0)	70.9 (7.7)	65.4 (8.1)	59.5 (10.6)	45.1 (13.0)	<0.001	56.2 (13.4)	67.2 (8.3)	61.0 (9.0)	54.2 (10.8)	42.9 (11.1)	<0.001
20–39	439 (11.8)	5 (0.5)	11 (1.2)	60 (6.5)	363 (38.2)		1218 (13.8)	21 (1.0)	53 (2.4)	227 (10.5)	917 (40.6)	
40–64	1517 (40.7)	134 (14.6)	356 (38.1)	519 (56.1)	508 (53.5)		4809 (54.7)	673 (30.6)	1287 (59.2)	1568 (72.4)	1281 (56.8)	
65–74	1351 (36.2)	494 (53.8)	476 (51.0)	312 (33.7)	69 (7.3)		2292 (26.1)	1132 (51.5)	762 (35.1)	340 (15.7)	58 (2.6)	
≥75	421 (11.3)	286 (31.1)	91 (9.7)	34 (3.7)	10 (1.1)		476 (5.4)	372 (16.9)	72 (3.3)	31 (1.4)	1 (0.0)	
Height (cm)	167.5 (6.3)	163.3 (5.5)	165.6 (5.1)	168.6 (5.3)	172.5 (5.3)	<0.001	155.8 (5.8)	151.7 (5.2)	154.4 (4.7)	156.9 (4.8)	160.1 (4.8)	<0.001
Weight (kg)	66.8 (10.2)	63.4 (9.1)	65.3 (9.2)	67.5 (9.5)	71.0 (11.3)	<0.001	54.2 (8.8)	52.4 (8.3)	53.5 (8.3)	54.8 (8.8)	56.2 (9.4)	<0.001
BMI (kg/m^2)	23.8 (3.1)	23.8 (2.9)	23.8 (3.0)	23.7 (2.9)	23.9 (3.5)	0.536	22.4 (3.5)	22.8 (3.5)	22.5 (3.4)	22.3 (3.4)	21.9 (3.5)	<0.001
SBP (mmHg)	133.9 (16.0)	138.9 (16.1)	136.3 (16.2)	133.0 (15.4)	127.6 (13.8)	<0.001	126.0 (17.8)	133.5 (17.5)	129.4 (17.1)	124.8 (17.2)	116.7 (14.7)	<0.001
DBP (mmHg)	80.9 (10.8)	78.8 (10.8)	81.5 (10.8)	82.5 (10.3)	80.8 (11.1)	<0.001	76.5 (10.5)	77.2 (10.4)	77.5 (10.4)	77.2 (10.6)	74.3 (10.4)	<0.001
Prevalence of hypertension (%)	1994 (53.5)	641 (69.7)	583 (62.4)	487 (52.6)	283 (29.8)	<0.001	2992 (34.0)	1144 (52.0)	877 (40.3)	655 (30.2)	316 (14.0)	<0.001
Glucose (mg/dl)	92.8 (20.8)	96.7 (24.8)	94.7 (21.6)	91.8 (19.0)	88.1 (15.8)	<0.001	86.8 (14.4)	90.2 (17.6)	87.9 (14.1)	85.8 (12.3)	83.3 (12.1)	<0.001
HbA1c (%)	5.6 (0.6)	5.8 (0.7)	5.7 (0.6)	5.6 (0.6)	5.4 (0.6)	<0.001	5.5 (0.5)	5.7 (0.6)	5.6 (0.5)	5.5 (0.4)	5.3 (0.4)	<0.001
Prevalence of diabetes (%)	389 (10.4)	156 (17.0)	113 (12.1)	77 (8.3)	43 (4.5)	<0.001	405 (4.6)	183 (8.3)	126 (5.8)	68 (3.1)	28 (1.2)	<0.001
TC (mg/dl)	201.3 (34.9)	197.7 (33.4)	201.6 (34.7)	203.8 (35.5)	202.2 (35.8)	0.002	212.4 (35.5)	216.0 (34.7)	219.1 (34.6)	215.3 (35.5)	199.8 (34.1)	<0.001
TG (mg/dl)	101.0 [72.0–149.0]	104.0 [73.5–147.5]	102.0 [76.0–152.0]	101.0 [71.0–147.0]	96.0 [66.3–146.0]	0.595	79.0 [58.0–112.0]	91.0 [67.0–124.0]	84.0 [62.0–119.0]	79.0 [58.0–109.0]	65.0 [49.0–90.0]	<0.001
HDL-C (mg/dl)	57.2 (15.1)	56.3 (14.9)	57.4 (15.8)	57.6 (14.7)	57.3 (15.2)	0.144	67.6 (16.2)	66.0 (16.3)	67.5 (16.2)	68.4 (16.5)	68.6 (15.8)	<0.001
Prevalence of hypercholesterolemia (%)	862 (23.1)	215 (23.4)	227 (24.3)	240 (25.9)	180 (18.9)	0.003	2749 (31.3)	887 (40.4)	827 (38.0)	686 (31.7)	349 (15.5)	<0.001
FEV_1 (l)	2.96 [2.56–3.43]	2.27 [2.03–2.42]	2.76 [2.66–2.85]	3.16 [3.06–3.29]	3.78 [3.58–4.04]	<0.001	2.26 [1.96–2.58]	1.76 [1.60– 1.86]	2.12 [2.04–2.18]	2.40 [2.33–2.48]	2.83 [2.69–3.03]	<0.001
FVC (l)	3.74 [3.28–4.26]	2.98 [2.71–3.20]	3.50 [3.32–3.70]	3.95 [3.76–4.15]	4.62 [4.34–4.95]	<0.001	2.78 [2.44–3.14]	2.22 [2.03–2.37]	2.63 [2.51–2.74]	2.93 [2.81–3.07]	3.37 [3.20–3.61]	<0.001
%VC (%)	101.9 (13.5)	93.4 (13.3)	101.2 (11.4)	105.2 (12.4)	107.6 (12.3)	<0.001	103.1 (13.6)	95.1 (12.6)	103.0 (12.2)	105.6 (13.0)	108.5 (12.9)	<0.001
Restrictive ventilatory impairment (%)	164 (4.4)	132 (14.4)	17 (1.8)	10 (1.1)	5 (0.5)	<0.001	285 (3.2)	206 (9.4)	36 (1.7)	34 (1.6)	9 (0.4)	<0.001
FEV_1/FVC (%)	79.0 (7.1)	74.2 (8.7)	78.7 (5.5)	80.4 (5.3)	82.7 (5.2)	<0.001	81.4 (5.8)	78.2 (6.5)	80.6 (4.7)	82.1 (4.9)	84.6 (5.1)	<0.001
Obstructive ventilatory impairment (%)	313 (8.4)	224 (24.4)	57 (6.1)	22 (2.4)	10 (1.1)	<0.001	249 (2.8)	186 (8.5)	34 (1.6)	25 (1.2)	4 (0.2)	<0.001
METs (MET-min/week)	91.5 [12.9–250.7]	138.0 [37.9–306.0]	126.0 [27.0–280.2]	90.0 [18.0–252.0]	36.0 [0.0–137.7]	<0.001	66.3 [8.4–192.9]	121.7 [28.9–252.0]	90.0 [16.8–222.3]	57.9 [3.0–165.6]	28.9 [0.0–126.0]	<0.001
WBC count (/μl)	5963. (1585)	6102 (1613)	5951 (1536)	5856. (1582)	5944 (1602)	0.015	5585 (1489)	5592 (1370)	5507 (1440)	5506 (1560)	5731 (1567)	<0.001
Sodium excretion (g/day)	3.0 (1.2)	3.0 (1.1)	3.0 (1.1)	3.0 (1.2)	3.0 (1.3)	0.281	2.5 (1.1)	2.4 (1.0)	2.5 (1.1)	2.5 (1.1)	2.8 (1.2)	<0.001
Potassium excretion (g/day)	1.4 (0.8)	1.3 (0.7)	1.4 (0.7)	1.4 (0.8)	1.5 (0.8)	<0.001	1.3 (0.8)	1.2 (0.7)	1.2 (0.7)	1.3 (0.7)	1.4 (0.9)	<0.001
Education status (%)						<0.001						<0.001
Below high school	2084 (55.9)	607 (66.1)	556 (59.5)	504 (54.5)	417 (43.9)		4837 (55.0)	1459 (66.4)	1287 (59.2)	1118 (51.6)	973 (43.1)	
Vocational school, junior college, or technical college	454 (12.2)	70 (7.6)	103 (11.0)	102 (11.0)	179 (18.8)		2847 (32.4)	557 (25.3)	677 (31.1)	779 (36.0)	834 (37.0)	
University or graduate school	1131 (30.3)	221 (24.0)	262 (28.1)	307 (33.2)	341 (35.9)		1005 (11.4)	135 (6.1)	186 (8.6)	253 (11.7)	431 (19.1)	
Others	18 (0.5)	8 (0.9)	4 (0.4)	2 (0.2)	4 (0.4)		31 (0.4)	15 (0.7)	4 (0.2)	6 (0.3)	6 (0.3)	
Unknown	41 (1.1)	13 (1.4)	9 (1.0)	10 (1.1)	9 (0.9)		75 (0.9)	32 (1.5)	20 (0.9)	10 (0.5)	13 (0.6)	
Smoking status (%)						<0.001						<0.001
Never-smoker	1077 (28.9)	257 (28.0)	257 (27.5)	269 (29.1)	294 (30.9)		6918 (78.7)	1906 (86.7)	1818 (83.6)	1658 (76.5)	1536 (68.1)	
Ex-smoker	1875 (50.3)	495 (53.9)	519 (55.6)	486 (52.5)	375 (39.5)		1203 (13.7)	183 (8.3)	214 (9.8)	348 (16.1)	458 (20.3)	
Current smoker	754 (20.2)	160 (17.4)	152 (16.3)	166 (17.9)	276 (29.1)		622 (7.1)	89 (4.0)	127 (5.8)	151 (7.0)	255 (11.3)	
Unknown	22 (0.6)	7 (0.8)	6 (0.6)	4 (0.4)	5 (0.5)		52 (0.6)	20 (0.9)	15 (0.7)	9 (0.4)	8 (0.4)	
Drinking status (%)						<0.001						<0.001
Never drinker	665 (17.8)	181 (19.7)	157 (16.8)	160 (17.3)	167 (17.6)		4573 (52.0)	1339 (60.9)	1184 (54.5)	1080 (49.9)	970 (43.0)	
Ex-drinker	143 (3.8)	59 (6.4)	35 (3.7)	24 (2.6)	25 (2.6)		164 (1.9)	37 (1.7)	38 (1.7)	37 (1.7)	52 (2.3)	
<23 g	1439 (38.6)	340 (37.0)	335 (35.9)	354 (38.3)	410 (43.2)		3295 (37.5)	704 (32.0)	786 (36.2)	853 (39.4)	952 (42.2)	
≥23 g	1468 (39.4)	336 (36.6)	403 (43.1)	384 (41.5)	345 (36.3)		736 (8.4)	106 (4.8)	157 (7.2)	194 (9.0)	279 (12.4)	
Unknown	13 (0.3)	3 (0.3)	4 (0.4)	3 (0.3)	3 (0.3)		27 (0.3)	12 (0.5)	9 (0.4)	2 (0.1)	4 (0.2)	
History of respiratory disease (%)												
Asthma	228 (6.1)	75 (8.2)	46 (4.9)	48 (5.2)	59 (6.2)	0.015	590 (6.7)	155 (7.1)	135 (6.2)	143 (6.6)	157 (7.0)	0.673
Chronic bronchitis	26 (0.7)	8 (0.9)	9 (1.0)	4 (0.4)	5 (0.5)	0.442	85 (1.0)	34 (1.5)	13 (0.6)	25 (1.2)	13 (0.6)	0.002
Chronic obstructive pulmonary disease	18 (0.5)	12 (1.3)	4 (0.4)	2 (0.2)	0 (0.0)	<0.001	9 (0.1)	7 (0.3)	1 (0.01)	1 (0.01)	0 (0.0)	0.003

Values are expressed as mean (standard deviation) or median [interquartile range] for continuous variables, or as number (%) for categorical variables. Hypertension was defined as SBP at least 140 mmHg and/or DBP at least 90 mmHg or receiving treatment for hypertension. Diabetes was defined as nonfasting glucose at least 200 mg/dl and/or HbA1c at least 6.5%, or receiving treatment for diabetes. Hypercholesterolemia was defined as TC at least 240 mg/dl and/or treatment for dyslipidemia. Restrictive ventilatory impairment was defined as reduced VC of <80% of predicted. Obstructive ventilatory impairment was defined as reduced a ration in FEV_1 to FVC of <70%. FEV_1, forced expiratory volume at 1 s; FVC, forced vital capacity; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; METS, metabolic equivalents; Q, quartile, TC, total cholesterol; TG, triglyceride; VC, vital capacity; WBC, white blood cell.

TABLE 2. Participant's characteristics according to forced vital capacity quartile

Variables	Men	The quartile groups of FVC (range)				*P* value	Women	The quartile groups of FVC (range)				*P* value
		Q1 (<3.28)	Q2 (3.28–3.73)	Q3 (3.74–4.26)	Q4 (≥4.26)			Q1 (<2.44)	Q2 (2.44–2.77)	Q3 (2.78–3.14)	Q4 (≥3.14)	
Number	3728	930	917	938	943		8795	2156	2194	2218	2227	
Age (year)	60.1 (14.0)	70.6 (7.9)	64.5 (9.7)	58.7 (11.4)	46.9 (13.8)	<0.001	56.2 (13.4)	66.8 (8.5)	60.2 (10.1)	53.3 (11.9)	44.8 (11.6)	<0.001
20–39	439 (11.8)	6 (0.6)	30 (3.3)	76 (8.1)	327 (34.7)		1218 (13.8)	26 (1.2)	95 (4.3)	316 (14.2)	781 (35.1)	
40–64	1517 (40.7)	155 (16.7)	352 (38.4)	520 (55.4)	490 (52.0)		4809 (54.7)	683 (31.7)	1265 (57.7)	1520 (68.5)	1341 (60.2)	
65–74	1351 (36.2)	494 (53.1)	433 (47.2)	310 (33.0)	114 (12.1)		2292 (26.1)	1098 (50.9)	746 (34.0)	345 (15.6)	103 (4.6)	
≥75	421 (11.3)	275 (29.6)	102 (11.1)	32 (3.4)	12 (1.3)		476 (5.4)	349 (16.2)	88 (4.0)	37 (1.7)	2 (0.1)	
Height (cm)	167.5 (6.3)	162.8 (5.3)	165.7 (5.0)	168.7 (5.1)	172.8 (5.1)	<0.001	155.8 (5.8)	151.3 (5.0)	154.4 (4.7)	156.9 (4.5)	160.4 (4.7)	<0.001
Weight (kg)	66.8 (10.2)	63.5 (9.4)	65.1 (9.1)	67.6 (10.3)	71.2 (10.5)	<0.001	54.2 (8.8)	52.5 (8.5)	53.5 (8.6)	54.4 (8.6)	56.6 (9.1)	<0.001
BMI (kg/m^2)	23.8 (3.1)	23.9 (3.0)	23.7 (2.9)	23.7 (3.2)	23.8 (3.2)	0.534	22.4 (3.5)	22.9 (3.6)	22.4 (3.5)	22.1 (3.4)	22.0 (3.4)	<0.001
SBP (mmHg)	133.9 (16.0)	138.2 (16.2)	136.7 (16.2)	132.7 (15.7)	128.2 (13.9)	<0.001	126.0 (17.8)	133.7 (17.6)	128.7 (17.2)	124.1 (17.3)	117.9 (15.1)	<0.001
DBP (mmHg)	80.9 (10.8)	78.5 (10.6)	82.0 (10.9)	82.2 (10.3)	81.0 (11.1)	<0.001	76.5 (10.5)	77.5 (10.4)	77.2 (10.5)	76.8 (10.6)	74.7 (10.3)	<0.001
Prevalence of hypertension (%)	1994 (53.5)	647 (69.6)	575 (62.7)	468 (49.9)	304 (32.2)	<0.001	2992 (34.0)	1138 (52.8)	865 (39.4)	634 (28.6)	355 (15.9)	<0.001
Glucose (mg/dl)	92.8 (20.8)	96.8 (24.7)	94.3 (22.4)	92.0 (18.5)	88.0 (15.4)	<0.001	86.8 (14.4)	90.7 (18.0)	87.5 (13.9)	85.7 (13.0)	83.4 (10.8)	<0.001
HbA1c (%)	5.6 (0.6)	5.8 (0.73)	5.6 (0.6)	5.6 (0.6)	5.4 (0.5)	<0.001	5.5 (0.5)	5.7 (0.6)	5.6 (0.5)	5.5 (0.5)	5.3 (0.3)	<0.001
Prevalence of diabetes (%)	389 (10.4)	160 (17.2)	108 (11.8)	85 (9.1)	36 (3.8)	<0.001	405 (4.6)	197 (9.1)	116 (5.3)	69 (3.1)	23 (1.0)	<0.001
TC (mg/dl)	201.3 (34.9)	197.7 (33.8)	201.9 (36.0)	204.0 (34.7)	201.7 (34.9)	0.007	212.4 (35.5)	216.2 (34.9)	218.0 (34.7)	213.7 (35.8)	202.1 (34.6)	<0.001
TG (mg/dl)	101.0 [72.0–149.0]	105.0 [74.0 –149.0]	100.0 [74.0 –147.0]	103.0 [72.0 –151.0]	95.0 [65.5 –144.0]	0.475	79.0 [58.0 –112.0]	92.0 [68.0 –128.0]	83.0 [62.0 –117.0]	77.0 [57.0 – 107.0]	66.0 [50.0 –94.0]	<0.001
HDL-C (mg/dl)	57.2 (15.1)	56.0 (14.9)	57.7 (15.5)	57.5 (15.1)	57.4 (14.9)	0.475	67.6 (16.2)	65.7 (16.2)	67.5 (16.0)	68.4 (16.4)	68.8 (16.2)	<0.001
Prevalence of hypercholesterolemia (%)	862 (23.1)	229 (24.6)	212 (23.1)	247 (26.3)	174 (18.5)	<0.001	2749 (31.3)	879 (40.8)	805 (36.7)	672 (30.3)	393 (17.6)	<0.001
FEV_1 (l)	2.96 [2.56 –3.43]	2.31 [2.04–2.51]	2.78 [2.63–2.94]	3.16 [2.99–3.35]	3.76 [3.51–4.04]	<0.001	2.26 [1.96–2.58]	1.76 [1.60–1.89]	2.12 [2.01–2.22]	2.40 [2.28–2.52]	2.82 [2.65–3.03]	<0.001
FVC (l)	3.74 [3.28–4.26]	2.97 [2.71–3.14]	3.51 [3.40–3.62]	3.98 [3.85–4.11]	4.63 [4.42–4.96]	<0.001	2.78 [2.44–3.14]	2.21 [2.03–2.33]	2.62 [2.53–2.69]	2.94 [2.85–3.03]	3.39 [3.25–3.61]	<0.001
%VC (%)	101.9 (13.5)	91.5 (12.3)	100.5 (10.8)	105.4 (11.2)	110.0 (12.0)	<0.001	103.1 (13.6)	93.8 (12.2)	101.8 (11.7)	105.1 (12.3)	111.2 (12.2)	<0.001
Restrictive ventilatory impairment (%)	164 (4.4)	141 (15.2)	18 (2.0)	3 (0.3)	2 (0.2)	<0.001	285 (3.2)	231 (10.7)	41 (1.9)	13 (0.6)	0 (0.0)	<0.001
FEV_1/FVC (%)	79.0 (7.1)	77.6 (8.9)	79.0 (6.5)	79.3 (6.3)	80.2 (6.0)	<0.001	81.4 (5.8)	80.3 (6.3)	81.1 (5.6)	81.7 (5.5)	82.4 (5.7)	<0.001
Obstructive ventilatory impairment (%)	313 (8.4)	126 (13.5)	76 (8.3)	66 (7.0)	45 (4.8)	<0.001	249 (2.8)	111 (5.1)	51 (2.3)	46 (2.1)	41 (1.8)	<0.001
METs (MET-min/week)	91.5 [12.9–250.7]	135.0 [36.0–302.5]	124.7 [30.0–284.8]	81.9 [9.2–238.8]	42.0 [0.0–156.9]	<0.001	66.3 [8.4–192.9]	112.5 [27.0–246.0]	88.9 [12.0–217.0]	57.9 [3.0–171.0]	33.7 [0.0, 126.5]	<0.001
WBC count (/μl)	5963 (1585)	6059 (1656)	5981 (1535)	5849 (1520)	5965 (1621)	0.075	5585 (1489)	5627 (1370)	5488 (1422)	5549 (1578)	5676 (1566)	<0.001
Sodium excretion (g/day)	3.0 (1.2)	3.0 (1.1)	3.0 (1.1)	3.0 (1.2)	3.1 (1.3)	0.281	2.5 (1.1)	2.5 (1.0)	2.4 (1.1)	2.6 (1.2)	2.7 (1.2)	<0.001
Potassium excretion (g/day)	1.4 (0.8)	1.4 (0.7)	1.4 (0.7)	1.4 (0.8)	1.5 (0.8)	0.002	1.3 (0.8)	1.2 (0.7)	1.2 (0.7)	1.3 (0.8)	1.4 (0.8)	<0.001
Education status (%)						<0.001						<0.001
Below high school	2084 (55.9)	618 (66.5)	542 (59.1)	503 (53.6)	421 (44.6)		4837 (55.0)	1430 (66.3)	1265 (57.7)	1156 (52.1)	986 (44.3)	
Vocational school, junior college, or technical college	454 (12.2)	78 (8.4)	88 (9.6)	120 (12.8)	168 (17.8)		2847 (32.4)	547 (25.4)	709 (32.3)	764 (34.4)	827 (37.1)	
University or graduate school	1131 (30.3)	214 (23.0)	275 (30.0)	298 (31.8)	344 (36.5)		1005 (11.4)	133 (6.2)	192 (8.8)	280 (12.6)	400 (18.0)	
Others	18 (0.5)	7 (0.8)	4 (0.4)	3 (0.3)	4 (0.4)		31 (0.4)	11 (0.5)	10 (0.5)	5 (0.2)	5 (0.2)	
Unknown	41 (1.1)	13 (1.4)	8 (0.9)	14 (1.5)	6 (0.6)		75 (0.9)	35 (1.6)	18 (0.8)	13 (0.6)	9 (0.4)	
Smoking status (%)						<0.001						<0.001
Never-smoker	1077 (28.9)	284 (30.5)	266 (29.0)	249 (26.5)	278 (29.5)		6918 (78.7)	1872 (86.8)	1858 (84.7)	1667 (75.2)	1521 (68.3)	
Ex-smoker	1875 (50.3)	493 (53.0)	494 (53.9)	494 (52.7)	394 (41.8)		1203 (13.7)	181 (8.4)	213 (9.7)	365 (16.5)	444 (19.9)	
Current smoker	754 (20.2)	148 (15.9)	150 (16.4)	188 (20.0)	268 (28.4)		622 (7.1)	81 (3.8)	111 (5.1)	177 (8.0)	253 (11.4)	
Unknown	22 (0.6)	5 (0.5)	7 (0.8)	7 (0.7)	3 (0.3)		52 (0.6)	22 (1.0)	12 (0.5)	9 (0.4)	9 (0.4)	
Drinking status (%)						<0.001						<0.001
Never drinker	665 (17.8)	199 (21.4)	148 (16.1)	149 (15.9)	169 (17.9)		4573 (52.0)	1332 (61.8)	1187 (54.1)	1091 (49.2)	963 (43.2)	
Ex-drinker	143 (3.8)	57 (6.1)	36 (3.9)	27 (2.9)	23 (2.4)		164 (1.9)	34 (1.6)	44 (2.0)	39 (1.8)	47 (2.1)	
<23 g	1439 (38.6)	346 (37.2)	342 (37.3)	361 (38.5)	390 (41.4)		3295 (37.5)	671 (31.1)	810 (36.9)	879 (39.6)	935 (42.0)	
≥23 g	1468 (39.4)	325 (34.9)	388 (42.3)	395 (42.1)	360 (38.2)		736 (8.4)	106 (4.9)	145 (6.6)	206 (9.3)	279 (12.5)	
Unknown	13 (0.3)	3 (0.3)	3 (0.3)	6 (0.6)	1 (0.1)		27 (0.3)	13 (0.6)	8 (0.4)	3 (0.1)	3 (0.1)	
History of respiratory disease (%)												
Asthma	228 (6.1)	65 (7.0)	45 (4.9)	51 (5.4)	67 (7.1)	0.115	590 (6.7)	143 (6.6)	139 (6.3)	151 (6.8)	157 (7.0)	0.812
Chronic bronchitis	26 (0.7)	8 (0.9)	7 (0.8)	6 (0.6)	5 (0.5)	0.840	85 (1.0)	29 (1.3)	21 (1.0)	19 (0.9)	16 (0.7)	0.176
Chronic obstructive pulmonary disease	18 (0.5)	6 (0.6)	7 (0.8)	4 (0.4)	1 (0.1)	0.182	9 (0.1)	6 (0.3)	2 (0.1)	0 (0.0)	1 (0.01)	0.023

Values are expressed as mean (standard deviation) or median (interquartile range) for continuous variables, or as number (%) for categorical variables.
Hypertension was defined as SBP at least 140 mmHg and/or DBP at least 90 mmHg or receiving treatment for hypertension. Diabetes was defined as nonfasting glucose at least 200 mg/dl and/or HbA1c at least 6.5% or receiving treatment for diabetes. Hypercholesterolemia was defined as TC at least 240 mg/dl and/or treatment for dyslipidemia. Restrictive ventilatory impairment was defined as reduced VC of less than 80% of predicted. Obstructive ventilatory impairment was defined as reduced a ration in FEV_1 to FVC of less than 70%. FEV_1, forced expiratory volume at 1 s; FVC, forced vital capacity; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; METS, metabolic equivalents; Q, quartile, TC, total cholesterol; TG, triglyceride; VC, vital capacity; WBC, white blood cell.

TABLE 3. Association between forced expiratory volume at 1 s and prevalence of hypertension

	The quartile groups of FEV_1 (range)				
Men	**Q1 (<2.56)**	**Q2 (2.56–2.95)**	**Q3 (2.96–3.43)**	**Q4 (≥3.43)**	
Number of participants	919	934	925	950	*P* for linear trend
Number of cases	641 (69.8)	583 (62.4)	487 (52.7)	283 (29.8)	
Crude	1.00 (reference)	0.72 (0.59–0.87)	0.48 (0.40–0.58)	0.18 (0.15–0.22)	<0.001
Model 1	1.00 (reference)	0.91 (0.75–1.12)	0.78 (0.62–0.96)	0.52 (0.40–0.69)	<0.001
Model 2	1.00 (reference)	0.90 (0.73–1.12)	0.79 (0.63–0.99)	0.54 (0.40–0.72)	<0.001
Model 3	1.00 (reference)	0.92 (0.74–1.13)	0.81 (0.64–1.02)	0.56 (0.42–0.75)	<0.001
	The quartile groups of FEV_1 (range)				
Women	**Q1 (<1.96)**	**Q2 (1.96–2.25)**	**Q3 (2.26–2.58)**	**Q4 (≥2.58)**	
Number of participants	2198	2174	2166	2257	*P* for linear trend
Number of case	1144 (52.1)	877 (40.3)	655 (30.2)	316 (14.0)	
Crude	1.00 (reference)	0.62 (0.55–0.70)	0.40 (0.35–0.45)	0.15 (0.13–0.17)	<0.001
Model 1	1.00 (reference)	0.94 (0.83–1.07)	0.93 (0.80–1.07)	0.72 (0.59–0.88)	0.006
Model 2	1.00 (reference)	0.93 (0.82–1.07)	0.91 (0.78–1.06)	0.69 (0.56–0.85)	0.003
Model 3	1.00 (reference)	0.94 (0.82–1.08)	0.93 (0.79–1.08)	0.70 (0.57–0.86)	0.005

Analysis by multivariable logistic regression model. Model 1 was adjusted for age (continuous), height (continuous), and educational status (below high school, vocational school, junior college, technical college, university or graduate school, others, unknown). Model 2 was adjusted for age, height, educational status, smoking status (never smoker, ex-smoker, current smoker, unknown), weight (continuous), diabetes, hypercholesterolemia, drinking status (never drinker, ex-drinker, current drinker, unknown), estimated 24-h sodium excretion, and potassium excretion. Model 3 was adjusted for Model 2 plus METs (quartile groups) and WBC count (quartile groups). The *P* values for the analysis of linear trends were calculated by scoring the FEV_1 category from 1 for the lowest to 4 for the highest, entering the number as a continuous term in the regression model. FEV_1, forced expiratory volume at 1 s; METs, metabolic equivalents; Q, quartile; WBC, white blood cell.

Table 3 shows the association between FEV_1 and prevalence of hypertension. We found that FEV_1 was inversely associated with the prevalence of hypertension (*P* for linear trend <0.001). Even with the addition of several potential confounders (METs and WBC count) at adjustments, these associations remained statistically significant. In model 3, for Q1 (reference), Q2, Q3, and Q4, the multivariate ORs were 1.00, 0.92 (0.74–1.13), 0.81 (0.64–1.02), and 0.56 (0.42–0.75) in men; and 1.00, 0.94 (0.82–1.08), 0.93 (0.79–1.08), and 0.70 (0.57–0.86) in women, respectively.

We also found that FVC was inversely associated with the prevalence of hypertension (*P* for linear trend <0.001). This association remained significant even after adjusting for several confounding variables. In model 3, for Q1 (reference), Q2, Q3, and Q4, the multivariate ORs were 1.00, 0.99 (0.80–1.22), 0.71 (0.57–0.90), and 0.59 (0.44–0.78) in men; and 1.00, 0.91 (0.80–1.04), 0.87 (0.74–1.01), and 0.69 (0.57–0.84) in women, respectively (Table 4).

Moreover, we performed an analysis with home hypertension as outcome. The prevalence of home hypertension was 1492 (59%) for men and 2187 (36%) for women. In the multivariable analysis, lower FEV_1 was significantly related to an increased prevalence of home hypertension. In model 3, the multivariate ORs were 1.00, 0.68 (0.52–0.88), 0.62 (0.47–0.82), and 0.40 (0.28–0.56) in men; and 1.00, 0.77 (0.66–0.91), 0.71 (0.59–0.86), 0.50 (0.39–0.64) in women,

TABLE 4. Association between forced vital capacity and prevalence of hypertension

	The quartile groups of FVC (range)				
Men	**Q1 (<3.28)**	**Q2 (3.28–3.73)**	**Q3 (3.74–4.26)**	**Q4 (≥4.26)**	
Number of participants	930	917	938	943	*P* for linear trend
Number of cases	647 (69.6)	575 (62.7)	468 (49.9)	304 (32.2)	
Crude	1.00 (reference)	0.74 (0.61–0.89)	0.44 (0.36–0.53)	0.21 (0.17–0.25)	<0.001
Model 1	1.00 (reference)	0.95 (0.78–1.17)	0.70 (0.56–0.87)	0.53 (0.40–0.69)	<0.001
Model 2	1.00 (reference)	0.98 (0.79–1.21)	0.70 (0.56–0.88)	0.57 (0.43–0.75)	<0.001
Model 3	1.00 (reference)	0.99 (0.80–1.22)	0.71 (0.57–0.90)	0.59 (0.44–0.78)	<0.001
	The quartile groups of FVC (range)				
Women	**Q1 (<2.44)**	**Q2 (2.44–2.77)**	**Q3 (2.78–3.14)**	**Q4 (≥3.14)**	
Number of participants	2156	2194	2218	2227	*P* for linear trend
Number of cases	1138 (52.8)	865 (39.4)	634 (28.6)	355 (15.9)	
Crude	1.00 (reference)	0.58 (0.52–0.66)	0.36 (0.32–0.41)	0.17 (0.15–0.20)	<0.001
Model 1	1.00 (reference)	0.88 (0.77–1.00)	0.82 (0.71–0.95)	0.67 (0.55–0.80)	<0.001
Model 2	1.00 (reference)	0.90 (0.79–1.03)	0.85 (0.73–0.99)	0.68 (0.56–0.83)	<0.001
Model 3	1.00 (reference)	0.91 (0.80–1.04)	0.87 (0.74–1.01)	0.69 (0.57–0.84)	<0.001

Analysis by multivariable logistic regression model. Model 1 was adjusted for age (continuous), height (continuous), and educational status (below high school, vocational school, junior college, technical college, university or graduate school, others, unknown). Model 2 was adjusted for age, height, educational status, smoking status (never smoker, ex-smoker, current smoker, unknown), weight (continuous), diabetes, hypercholesterolemia, drinking status (never drinker, ex-drinker, current drinker, unknown), estimated 24-h sodium excretion, and potassium excretion. Model 3 was adjusted for Model 2 plus METs (quartile groups) and WBC count (quartile groups). The *P* values for the analysis of linear trends were calculated by scoring the FVC category from 1 for the lowest to 4 for the highest, entering the number as a continuous term in the regression model. FVC, forced vital capacity; METs, metabolic equivalents; Q, quartile; WBC, white blood cell.

TABLE 5. Association between forced expiratory volume at 1 s and prevalence of home hypertension

Men	The quartile groups of FEV_1 (range)				
	Q1 (<2.53)	Q2 (2.53–2.89)	Q3 (2.90–3.30)	Q4 (>3.30)	
Number of participants	623	638	625	640	*P* for linear trend
Number of case	467 (75.0)	410 (64.3)	363 (58.1)	252 (39.4)	
Crude	1.00 (reference)	0.60 (0.47–0.77)	0.46 (0.36–0.59)	0.22 (0.17–0.28)	<0.001
Model 1	1.00 (reference)	0.68 (0.53–0.87)	0.58 (0.45–0.76)	0.36 (0.45–0.76)	<0.001
Model 2	1.00 (reference)	0.67 (0.52–0.87)	0.60 (0.45–0.78)	0.38 (0.27–0.53)	<0.001
Model 3	1.00 (reference)	0.68 (0.52–0.88)	0.62 (0.47–0.82)	0.40 (0.28–0.56)	<0.001
Women	**The quartile groups of FEV_1 (range)**				
	Q1(<1.94)	Q2(1.94–2.24)	Q3(2.25–2.55)	Q4(>2.55)	
Number of participants	1490	1563	1523	1543	*P* for linear trend
Number of case	849 (73.9)	652 (41.7)	467 (30.7)	219 (14.2)	
Crude	1.00 (reference)	0.54 (0.47–0.62)	0.33 (0.29–0.39)	0.12 (0.10–0.15)	<0.001
Model 1	1.00 (reference)	0.78 (0.67–0.91)	0.73 (0.61–0.87)	0.53 (0.42–0.66)	<0.001
Model 2	1.00 (reference)	0.76 (0.65–0.90)	0.69 (0.58–0.84)	0.49 (0.38–0.62)	<0.001
Model 3	1.00 (reference)	0.77 (0.66–0.91)	0.71 (0.59–0.86)	0.50 (0.39–0.64)	<0.001

Analysis by multivariable logistic regression model. Home hypertension was defined as morning home SBP at least 135 mmHg, and/or home DBP at least 85 mmHg, and/or self-reported treatment for hypertension. Model 1 was adjusted for age (continuous), height (continuous), and educational status (below high school; vocational school, junior college, or technical college; university or graduate school; others; unknown). Model 2 was adjusted for age, height, educational status (below high school; vocational school, junior college, or technical college; university or graduate school; others; unknown), smoking status (never-smoker, ex-smoker, current smoker, unknown), weight (continuous), diabetes, hypercholesterolemia, drinking status (never drinker, ex-drinker, < 23 g, ≥ 23 g, unknown) and estimated 24-h sodium excretion, and potassium excretion. Model 3 was adjusted as for model 2 plus METs (quartile category) and WBC count (quartile category). The *P* values for the analysis of linear trends were calculated by scoring the FEV_1 category from 1 for the lowest to 4 for the highest, entering the number as a continuous term in the regression model. cIMT carotid intima–media thickness; FEV_1, forced expiratory volume at 1 s; METs, metabolic equivalents; Q, quartile; WBC, white blood cell.

respectively (Table 5). Similarly, FVC was inversely associated with the prevalence of home hypertension. In model 3, the multivariate ORs were 1.00, 0.81 (0.62–1.05), 0.62 (0.47–0.82), 0.41 (0.29–0.58) in men; and 1.00, 0.79 (0.67–0.93), 0.69 (0.58–0.84), 0.50 (0.40–0.64) in women, respectively (Table 6).

Several sensitivity analyses were conducted. First, we performed stratified analysis by smoking status. FEV_1 and FVC were inversely associated with the prevalence of hypertension in both men and women even among never-smoker (e-Tables 1 and 2, http://links.lww.com/HJH/C118). These association was also confirmed among ex-smokers (e-Tables 3 and 4, http://links.lww.com/HJH/C118). In current smoker, an inverse association between lung function and hypertension was observed in men but not in women (e-Tables 5 and 6, http://links.lww.com/HJH/C118). Second, we conducted analysis stratified by age. In general, the highest quartile of FEV_1 showed a lower OR for hypertension than the lowest quartile. In terms of *P* for trend, FEV_1 was inversely and significantly associated

TABLE 6. Association between forced vital capacity and prevalence of home hypertension

Men	The quartile groups of FVC (range)				
	Q1 (<3.25)	Q2 (3.25–3.68)	Q3 (3.69–4.17)	Q4 (>4.17)	*P* for linear trend
Number of participants	617	637	635	637	
Number of cases	456 (73.9)	420 (65.9)	359 (56.5)	257 (40.4)	
Crude	1.00 (reference)	0.68 (0.54–0.87)	0.46 (0.36–0.58)	0.24 (0.19–0.30)	<0.001
Model 1	1.00 (reference)	0.77 (0.60–0.99)	0.58 (0.44–0.75)	0.37 (0.27–0.51)	<0.001
Model 2	1.00 (reference)	0.79 (0.61–1.03)	0.60 (0.46–0.80)	0.40 (0.28–0.56)	<0.001
Model 3	1.00 (reference)	0.81 (0.62–1.05)	0.62 (0.47–0.82)	0.41 (0.29–0.58)	<0.001
Women	**The quartile groups of FVC (range)**				
	Q1 (<2.43)	Q2 (2.43–2.76)	Q3 (2.77–3.10)	Q4 (>3.10)	*P* for linear trend
Number of participants	1500	1503	1551	1565	
Number of cases	862 (57.5)	622 (41.4)	455 (29.3)	248 (15.9)	
Crude	1.00 (reference)	0.52 (0.45–0.60)	0.31 (0.26–0.36)	0.14 (0.12–0.16)	<0.001
Model 1	1.00 (reference)	0.76 (0.65–0.89)	0.64 (0.54–0.77)	0.48 (0.38–0.59)	<0.001
Model 2	1.00 (reference)	0.78 (0.66–0.92)	0.67 (0.56–0.81)	0.49 (0.39–0.61)	<0.001
Model 3	1.00 (reference)	0.79 (0.67–0.93)	0.69 (0.58–0.84)	0.50 (0.40–0.64)	<0.001

Analysis by multivariable logistic regression model. Home hypertension was defined as morning home SBP at least 135 mmHg, and/or home DBP at least 85 mmHg, and/or self-reported treatment for hypertension. Model 1 was adjusted for age (continuous), height (continuous), and educational status (below high school; vocational school, junior college, or technical college; university or graduate school; others; unknown). Model 2 was adjusted for age, height, educational status (below high school; vocational school, junior college, or technical college; university or graduate school; others; unknown), smoking status (never-smoker, ex-smoker, current smoker, unknown), weight (continuous), diabetes, hypercholesterolemia, drinking status (never drinker, ex-drinker, less than 23 g, at least 23 g, unknown) and estimated 24 h sodium excretion, and potassium excretion. Model 3 was adjusted for model 2 plus METs (quartile category) and WBC count (quartile category). The *P* values for the analysis of linear trends were calculated by scoring the FVC category from 1 for the lowest to 4 for the highest, entering the number as a continuous term in the regression model. FVC, forced vital capacity; METs, metabolic equivalents; Q, quartile; WBC, white blood cell.

with the prevalence of hypertension among middle-aged, elderly, and very old men (e-Tables 7–10, http://links.lww.com/HJH/C118). In women, FEV_1 was inversely and significantly associated with age only in middle-aged participants. Similarly, in FVC, an inverse and significant association was observed among middle-aged, elderly, and very old men as well as in middle-aged women (e-Tables 11–14, http://links.lww.com/HJH/C118). Third, we excluded participants with respiratory diseases. Consequently, FEV_1 and FVC were inversely associated with the prevalence of hypertension in men and women (e-Tables 15 and 16, http://links.lww.com/HJH/C118). Fourth, when we excluded participants' treatment for hypertension, FEV_1 was inversely associated with the prevalence of hypertension among men but not in women (e-Tables 17, http://links.lww.com/HJH/C118). For FVC, an inverse association was observed in both men and women (e-Tables 18, http://links.lww.com/HJH/C118).

DISCUSSION

The present study showed that higher lung function was associated with a lower prevalence of hypertension in the Japanese population, even after adjustment for several potential confounders. These inverse associations were also observed among never-smokers. Furthermore, reduced lung function was also associated with higher prevalence of home hypertension.

Several studies have examined the association between lung function and hypertension. A normative aging study reported a significantly inverse association between FVC and the incidence of hypertension [6]. The People's Republic of China-United States cardiopulmonary epidemiologic study showed an inverse association between FVC and FEV_1 and hypertension [8]. In the Seattle Nikkei Health Study, poor lung function was significantly associated with the prevalence of hypertension in a Japanese American population [10]. The Coronary Artery Risk Development in Young Adults Study reported that a decline in FVC is inversely associated with the incidence of hypertension [12]. Our results showed that FEV_1 and FVC were inversely associated with the prevalence of hypertension, which is consistent with the results of previous studies.

In the additional analyses of the association between lung function and home hypertension, we showed that reduced lung function was associated with higher prevalence of home hypertension. Previous studies have reported that home BP have strong prediction of the risk of cardiovascular disease when compared with casual BP [22–25]. This is because home BP might avoid regression dilution bias and the white-coat effect [22,23,34,35,44,45]. However, no study has investigated the association between lung function and home hypertension, our results extend previous findings of the association between lung function and hypertension.

Although this observational study could not clarify the potential mechanisms of our findings, we raised some possibilities of confounding and performed stratified analysis. First, smoking may have been an important confounding factor. Several previous studies have shown that lung function is related to cardiovascular disease even among nonsmokers [1–3]. However, only a few studies have examined the association between lung function and hypertension among never-smokers [7,8]. The Cardiovascular Health Study showed that lung function is inversely associated with hypertension while excluding participants with a history of current smoking and ex-smokers of at least 20 pack-years [7]. In the People's Republic of China-United States cardiopulmonary epidemiologic study, lung function was inversely related to BP even among never-smokers [8]. Similar to previous studies, this study showed an inverse association even among never-smokers. Thus, we considered that the inverse association between lung function and hypertension might be independent of the smoking status.

Second, age-related confounding is a possibility. Both BP and respiratory function were strongly associated with age [10,15,19,20]. Moreover, the age-related decrease in elastic recoil might influence decreased vital capacity [21]. Therefore, we conducted stratified analysis based on age. In general, participants in the highest quartile of lung function showed lower odds of hypertension among all age–sex subgroups. Even in the stratified subgroups, lung function was inversely and significantly associated with the prevalence of hypertension among middle-aged, elderly, and very old men. In women, lung function was inversely associated with the prevalence of hypertension in middle-aged participants. Third, weight may be a common factor underlying decreased lung function and increased BP [46,47]. In this study, even after adjusting for weight, an inverse association between lung function and hypertension was observed. Therefore, we considered that the inverse association between lung function and hypertension might be independent of the smoking status, age and weight. Fourth, physical activity may explain the association between lung function and the prevalence of hypertension. Many previous studies have shown that physical activity is associated with increased lung function and a decreased risk of hypertension [48,49]. However, even after adjusting for physical activity, lung function was inversely associated with the prevalence of hypertension. Inflammation is also considered to be a potential mechanism. Several previous studies have shown that reduced lung function is associated with increased levels of markers of inflammation [50–54]. Additionally, high levels of markers of inflammation, including circulating C-reactive protein (CRP), high-sensitivity CRP, interleukin 6, and WBC count were associated with an increased risk of hypertension [53,54]. Although we adjusted for WBC count, an inverse association between lung function and hypertension remained. To elucidate the contribution of inflammation, further studies are warranted using detailed inflammatory markers such as CRP and interleukin 6.

Other potentially harmful mechanisms might be considered. The lungs are a major organ that expresses high levels of angiotensin-converting enzyme (ACE) 1 and ACE2, which play important roles in the renin–angiotensin system [55,56]. Renin converts angiotensinogen to angiotensin I. ACE1 removes the carboxy-terminal dipeptide from the angiotensin I to produce the potent vasoconstrictor angiotensin II and degrades the vasodilator bradykinin [55,56,57]. Conversely, ACE2 converts angiotensin II to the vasodilators angiotensin 1–7 thereby reducing BP [56,58–60]. These might contribute the association between lung function and

hypertension, though, as far as we know, there is no study to explain the clear mechanism of this association in terms of ACEs. Further studies are required to elucidate the potential mechanisms underlying respiratory function and hypertension.

This study has several strengths. First, this was a large population-based cohort study, which allowed stratification by confounding factors including smoking status and included various confounding factors such as sodium and potassium excretion. Second, to the best of our knowledge, this is the first study to show an association between lung function and hypertension based on casual BP and home BP. Furthermore, this is also the first study to show an association between lung function and hypertension in the Japanese population.

Our study has several limitations. First, lung function might have been measured with some errors because lung function is dependent on the effort of the participants. Second, although we restricted never-smokers to eliminate the effects of smoking, we could not completely eliminate the effects of smoking because never-smokers included participants who had smoked less than 100 cigarettes in their lifetime. Third, lung function and prevalence of hypertension vary with ethnicity [61,62]. As this study included only the Japanese population, it is difficult to apply our results to other races. Fourth, as we did not collect the fasting blood samples and information on detailed inflammatory marker such as interleukin 6, tumor necrosis factor-α, and C-reactive protein, further studies using fasting blood samples and detailed inflammatory marker may be preferable. Finally, we could not confirm causal relationships as this was a cross-sectional study. Prospective cohort studies are warranted to clarify the causal relationships.

In conclusion, this study showed that reduced lung function was significantly associated with an increased prevalence of hypertension in the Japanese population after adjusting for several potential confounding factors. This association was observed among never-smokers. Additionally, we found that reduced lung function was significantly associated with an increased prevalence of home hypertension. Therefore, participants with reduced lung function or hypertension, especially middle-aged, elderly, and very old men and middle-aged women, might be required to measure their lung function or BP.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Schroeder EB, Welch VL, Couper D, Nieto FJ, Liao D, Rosamond WD, Heiss G. Lung function and incident coronary heart disease: the Atherosclerosis Risk in Communities Study. *Am J Epidemiol* 2003; 158:1171–1181.
2. Sin DD, Wu L, Paul-Man SF. The relationship between reduced lung function and cardiovascular mortality: a population-based study and a systematic review of the literature. *Chest* 2005; 127:1952–1959.
3. Hozawa A, Billings JL, Shahar E, Ohira T, Rosamond WD, Folsom AR. Lung function and ischemic stroke incidence: the Atherosclerosis Risk in Communities study. *Chest* 2006; 130:1642–1649.
4. Wang B, Zhou Y, Xiao L, Guo Y, Ma J, Zhou M, *et al*. Association of lung function with cardiovascular risk: a cohort study. *Respir Res* 2018; 19:214.
5. WHO. Hypertension. Available at: https://www.paho.org/en/topics/hypertension. [Accessed 4 January 2022]
6. Sparrow D, Weiss ST, Vokonas PS, Cupples LA, Ekerdt DJ, Colton T. Forced vital capacity and the risk of hypertension. The normative aging study. *Am J Epidemiol* 1988; 127:734–741.
7. Enright PL, Kronmal RA, Smith VE, Gardin JM, Schenker MB, Manolio TA. Reduced vital capacity in elderly persons with hypertension, coronary heart disease, or left ventricular hypertrophy. The cardiovascular health study. *Chest* 1995; 107:28–35.
8. Wu Y, Vollmer WM, Buist AS, Tsai R, Cen R, Wu X, *et al*. Relationship between lung function and blood pressure in Chinese men and women of Beijing and Guangzhou. PRC-USA Cardiovascular and Cardiopulmonary Epidemiology Research Group. *Int J Epidemiol* 1998; 27:49–56.
9. Engstrom G, Wollmer P, Valind S, Hedblad B, Janzon L. Blood pressure increase between 55 and 68 years of age is inversely related to lung function: longitudinal results from the cohort study 'Men born in 1914'. *J Hypertens* 2001; 19:1203–1208.
10. Taneda K, Namekata T, Hughes D, Suzuki K, Knopp R, Ozasa K. Association of lung function with atherosclerotic risk factors among Japanese Americans: Seattle Nikkei health study. *Clin Exp Pharmacol Physiol* 2004; 31:S31–S34.
11. Schnabel E, Nowak D, Brasche S, Wichmann HE, Heinrich J. Association between lung function, hypertension and blood pressure medication. *Respir Med* 2011; 105:727–733.
12. Jacobs DR Jr, Yatsuya H, Hearst MO, Thyagarajan B, Kalhan R, Rosenberg S, *et al*. Rate of decline of forced vital capacity predicts future arterial hypertension: The coronary artery risk development in young adults study. *Hypertension* 2012; 59:219–225.
13. Karunanayake C, Rennie DC, Pahwa PM, Chen Y, Dosman JA. Relationship between lung function and hypertension among rural Canadians using fractional polynomials. *Sri Lankan J Appl Stat* 2012; 12:41–61.
14. Shah CH, Reed RM, Liang Y, Zafari Z. Association between lung function and future risks of diabetes, asthma, myocardial infarction, hypertension and all-cause mortality. *ERJ Open Res* 2021; 7:00178–2021.
15. Yohannes AM, Tampubolon G. Changes in lung function in older people from the English longitudinal study of aging. *Expert Rev Respir Med* 2014; 8:515–521.
16. Bowman TS, Gaziano JM, Buring JE, Sesso HD. A prospective study of cigarette smoking and risk of incident hypertensin in women. *J Am Coll Cardiol* 2007; 50:2085–2092.
17. Halperin RO, Gaziano JH, Sesso HD. Smoking and the risk of incident hypertension in middle-aged and older men. *Am J Hypertens* 2008; 21:148–152.
18. Kaplan RC, Baldoni PL, Strizich GM, Pérez-Stable EJ, Saccone NL, Peralta CA, *et al*. Current smoking raises risk of incident hypertension: Hispanic community health study-study of Latinos. *Am J Hypertens* 2021; 34:190–197.
19. Skloot GS. The effects of aging on lung structure and function. *Clin Geriatr Med* 2017; 33:447–457.
20. Buford TW. Hypertension and aging. *Aging Res Rev* 2016; 26:96–111.
21. Taylor BJ, Johnson BD. The pulmonary circulation and exercise responses in the elderly. *Semin Respir Crit Care Med* 2010; 31:528–538.

22. Ohkubo T, Imai Y, Tsuji I, Nagai K, Kato J, Kikuchi N, *et al.* Home blood pressure measurement has a stronger predictive power for mortality than dose screening blood pressure measurement: a population-based observation in Ohasama, Japan. *J Hypertens* 1998; 16:971–975.
23. Hozawa A, Ohkubo T, Nagai K, Kikuya M, Matsubara M, Tsuji I, *et al.* Prognosis of isolated systolic blood pressure and isolated diastolic hypertension as assessed by self-measurement of blood pressure at home: the Ohasama study. *Arch Intern Med* 2000; 160:3301–3306.
24. Niiranen T, Hanninen MR, Johansson J, Reunanen A, Jula AM. Home-measured blood pressure is a stronger predictor of cardiovascular risk than office blood pressure: The Finn-home study. *Hypertension* 2010; 55:1346–1351.
25. Bliziotis IA, Destounis A, Stergious GS. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: a systematic review and meta-analysis. *J Hypertens* 2012; 30:1289–1299.
26. Hozawa A, Tanno K, Nakaya N, Nakamura T, Tsuchiya N, Hirata T, *et al.* Study profile of the Tohoku medical Megabank community-based cohort study. *J Epidemiol* 2021; 31:65–76.
27. Kuriyama S, Yaegashi N, Nagami F, Arai T, Kawaguchi Y, Osumi N, *et al.* The Tohoku medical Megabank project: design and mission. *J Epidemiol* 2016; 26:493–511.
28. Nakaya N, Xie T, Scheerder B, Tsuchiya N, Narita A, Nakamura T, *et al.* Spousal similarities in cardiovascular risk factors: a cross-sectional comparison between Dutch and Japanese data from two large biobank studies. *Atherosclerosis* 2021; 334:85–92.
29. Hirata T, Kogure M, Tsuchiya N, Miyagawa K, Narita A, Nochioka K, *et al.* Impacts of the urinary sodium-to-potassium ratio, sleep efficiency, and conventional risk factors on home hypertension in a general Japanese population. *Hypertens Res* 2021; 44:858–865.
30. Takase M, Nakamura T, Tsuchiya N, Kogure M, Itabashi F, Narita A, *et al.* Association between the combined fat mass and fat-free mass index and hypertension: the Tohoku Medical Megabank community-based cohort study. *Clin Exp Hypertens* 2021; 43:610–621.
31. Takase M, Nakamura T, Hirata T, Tsuchiya N, Kogure M, Itabashi F, *et al.* Association between fat mass index, fat-free mass index, and hemoglobin A1c in a Japanese population: the Tohoku medical Megabank community-based cohort study. *J Diabetes Investig* 2021; 13:858–867.
32. Yamada M, Motoike IN, Kojima K, Fuse N, Hozawa A, Kuriyama S, *et al.* Genetic loci for lung function in Japanese adults with adjustment for exhaled nitric oxide levels as airway inflammation indicator. *Commun Biol* 2021; 4:1288.
33. Nishimoto Y, Tsubono Y, Kogure M, Nakamura T, Itabashi F, Tsuchiya N, *et al.* The prevalence of current smokers and alcohol drinkers among cancer survivors and subjects with no history of cancer among participants in a community-based cardiometabolic screening program in Miyagi prefecture, Japan: a comparison with nationally representative surveys in other countries. *Cancer Med* 2021; 10:9000–9011.
34. Kogure M, Hirata T, Nakaya N, Tsuchiya N, Nakamura T, Narita A, *et al.* Multiple measurements of the urinary sodium-to-potassium ratio strongly related home hypertension: TMM Cohort Study. *Hypertens Res* 2020; 43:62–71.
35. Hirata T, Nakamura T, Kogure M, Tsuchiya N, Narita A, Miyagawa K, *et al.* Reduced sleep efficiency, measured using an objective device, was related to an increased prevalence of home hypertension in Japanese adults. *Hypertens Res* 2020; 43:23–29.
36. Asayama K, Satoh M, Kikuya M. Diurnal blood pressure changes. *Hypertens Res* 2018; 41:669–678.
37. PhenX Toolkit, Research domain – alcohol, tobacco and other substances. Available at: https://www.phenxtoolkit.org/domains/view/3000#tab5content. [Accessed 28 November 2021]
38. Inoue M, Nagata C, Tsuji I, Sugawara Y, Wakai K, Tamakoshi A, *et al.*, Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan. Impact of alcohol intake on total mortality and mortality from major causes in Japan: a pooled analysis of six large-scale cohort studies. *J Epidemiol Community Health* 2021; 66:448–456.
39. Kikuchi H, Inoue S, Odagiri Y, Ihira H, Inoue M, Sawada N, *et al.* Intensity-specific validity and reliability of the Japan public health center-based prospective study-physical activity questionnaire. *Prev Med Rep* 2020; 20:101169.
40. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18:499–502.
41. Jacobs D, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, *et al.* Report of the conference on low blood cholesterol: Mortality associations. *Circulation* 1992; 86:1040–1060.
42. Tanaka T, Okamura T, Miura K, Kadowaki T, Ueshima H, Nakagawa H, Hashimoto T. A simple method to estimate populational 24-h urinary sodium and potassium excretion using a casual urine specimen. *J Hum Hypertens* 2002; 16:97–103.
43. Schnabel E, Karrasch S, Schulz H, Gläser S, Meisinger C, Heier M, *et al.*, Cooperative Health Research in the Region of Augsburg (KORA) Study Group. High blood pressure, antihypertensive medication and lung function in a general adult population. *Respir Res* 2011; 12:50.
44. James GD, Pickering TG, Yee LS, Harshfield GA, Riva J, Laragh JH. The reproducibility of average ambulatory, home, and clinic pressures. *Hypertension* 1988; 11:545–549.
45. Sakuma M, Imai Y, Nagai K, Watanabe N, Sakuma H, Minami N, *et al.* Reproducibility of home blood pressure measurements over a 1-year period. *Am J Hypertens* 1997; 10:798–803.
46. Chen Y, Horne SL, Dosman JA. Body weight and weight gain related to pulmonary function decline in adults: a six year follow up study. *Thorax* 1993; 48:375–380.
47. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension* 2003; 42:878–884.
48. Luzak A, Karrasch S, Thorand B, Nowak D, Holle R, Peters A, *et al.* Association of physical activity with lung function in lung-healthy German adults: results from the KORAFF4 study. *BMC Pulm Med* 2017; 17:215.
49. Liu X, Zhang D, Liu Y, Sun X, Han C, Wang B, *et al.* Dose-response association between physical activity and incident hypertension: a systematic review and meta-analysis of cohort studies. *Hypertension* 2017; 69:813–820.
50. Jiang R, Burke GL, Enright PL, Newman AB, Margolis HG, Cushman M, *et al.* Inflammatory markers and longitudinal lung function decline in the elderly. *Am J Epidemiol* 2008; 168:602–610.
51. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J* 2009; 33:1165–1185.
52. Wu X, Wang C, Li H, Meng H, Jie J, Fu M, *et al.* Circulating white blood cells and lung function impairment: the observational studies and Mendelian randomization analysis. *Ann Med* 2021; 53:1118–1128.
53. Jayedi A, Rahimi K, Rahimi K, Bautista LE, Nazarzadeh M, Zargar MS, Shab-Bidar S. Inflammation markers and risk of developing hypertension: a meta-analysis of cohort studies. *Heart* 2019; 105:686–692.
54. Ishida S, Kondo S, Funakoshi S, Satoh A, Maeda T, Kawazoe M, *et al.* White blood cell count and incidence of hypertension in the general Japanese population: ISSA-CKD study. *PLoS One* 2021; 16:e0246304.
55. Tipnis SR, Hooper NM, Hyde R, *et al.* A human homolog of angiotensin-converting enzyme. Cloning and functional expression as a captopril-insensitive carboxypeptidase. *J Biol Chem* 2000; 275:33238–33243.
56. Donoghue M, Hsieh F, Baronas E, Godbout K, Gosselin M, Stagliano N, *et al.* A novel angiotensin-converting enzyme–related carboxypeptidase (ACE2) converts angiotensin I to angiotensin 1-9. *Circ Res* 2000; 87:E1–E9.
57. Riet LT, Esch JHM, Roks AJM, Meiracker AH, Danser AHJ. Hypertension: renin-angiotensin-aldosterone system alterations. *Circ Res* 2015; 116:960–975.
58. Keidar S, Kaplan M, Gamliel-Lazarovich A. ACE2 of the heart: From angiotensin I to angiotensin (1-7). *Cardiovasc Res* 2007; 73:463–469.
59. Wang W, McKinnie SMK, Farhan M, Paul M, McDonald T, McLean B, *et al.* Angiotension-converting enzyme 2 metabolizes and partially inactivates Pyr-Apelin-13 and Apelin-17: physiological effects in the cardiovascular system. *Hypertension* 2016; 68:365–377.
60. Chamsi-Pasha MAR, Shao Z, Tang WH. Angiotensin-converting enzyme 2 as a therapeutic target for heart failure. *Curr Heart Fail Rep* 2014; 11:58–63.
61. Tipnis SR, Hooper NM, Hyde R, Karran E, Christie G, Turner AJ. Multiethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012; 40:1324–1343.
62. Tsugane S. Why has Japan become the world's most long-lived country: insights from a food and nutrition perspective. *Eur J Clin Nutr* 2021; 75:921–928.