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Journal

Clinical Cardiology, 41(7)

ISSN

0160-9289

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Publication Date

2018-07-01

DOI

10.1002/clc.22985

Peer reviewed

Received: 26 February 2018 | Revised: 19 May 2018 | Accepted: 23 May 2018

DOI: 10.1002/clc.22985

WILEY CLINICAL CARDIOLOGY

CLINICAL INVESTIGATIONS

Impact of lung-function measures on cardiovascular disease events in older adults with metabolic syndrome and diabetes

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Funding information
This research was supported by contracts HHSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, and N01HC85086, and grants U01HL080295 and U01HL130114, from the National Heart, Lung, and Blood Institute, with additional contribution from the National Institute of Neurological Disorders and Stroke. Additional support was provided by R01AG023629 from the National Institute on Aging. A full list of Cardiovascular Health Study principal investigators and institutions can be found at http://www.CHS-NHLBI.org. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Background: Individuals with metabolic syndrome (MetS) and diabetes (DM) are more likely to have decreased lung function and are at greater risk of cardiovascular disease (CVD).

Hypothesis.: Lung-function measures can predict CVD events in older persons with MetS, DM, and neither condition.

Methods: We followed 4114 participants age ≥ 65 years with and without MetS or DM in the Cardiovascular Health Study. Cox regression examined the association of forced vital capacity (FVC) and 1-second forced expiratory volume (FEV_1; percent of predicted values) with incident coronary heart disease and CVD events over 12.9 years.

Results: DM was present in 537 (13.1%) and MetS in 1277 (31.0%) participants. Comparing fourth vs first quartiles for FVC, risk of CVD events was 16% (HR: 0.84, 95% CI: 0.59–1.18), 23% (HR: 0.77, 95% CI: 0.60–0.99), and 30% (HR: 0.70, 95% CI: 0.58–0.84) lower in DM, MetS, and neither disease groups, respectively. For FEV_1, CVD risk was lower by 2% (HR: 0.98, 95% CI: 0.70–1.37), 26% (HR: 0.74, 95% CI: 0.59–0.93), and 31% (HR: 0.69, 95% CI: 0.57–0.82) in DM. Findings were strongest for predicting congestive heart failure (CHF) in all disease groups. C-statistics increased significantly with addition of FEV_1 or FVC over risk factors for CVD and CHF among those with neither MetS nor DM.

Conclusions: FEV_1 and FVC are inversely related to CVD in older adults with and without MetS, but not DM (except for CHF); however, their value in incremental risk prediction beyond standard risk factors is limited mainly to metabolically healthier persons.

KEYWORDS

Cardiovascular, Cox Regression, Diabetes, Lung Function, Metabolic Syndrome

1 | INTRODUCTION

Previous studies have identified decreased lung function as an independent prognostic predictor for CVD events, and this effect appears to be more pronounced in women than in men.[1–4] In addition, both cross-sectional and prospective studies show an association of reduced lung function with MetS and DM.[5–11] We have previously shown in the Third National Health and Nutrition Examination Survey

(NHANES III) reduced lung function to be associated with total mortality among persons with MetS and DM.[12] Also, the spirometric variables of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) add incremental value in predicting total mortality among intermediate-risk Framingham Risk Score individuals.[13]

Those with MetS and DM are also more likely to have subclinical atherosclerosis and are at a greater risk of CVD.[14–16] However, whether reduced lung function in these groups may further refine prediction of CVD events is unclear. Such information would be useful to judge the utility of lung-function assessment as an independent predictor of future CVD events and mortality in these groups.

This study examined whether spirometric measures of lung function predict CVD events and their components among higher-risk individuals among those with MetS and DM. We hypothesized that lung-function measurements are related to the risk of future CVD events in these groups.

2 | METHODS

The Cardiovascular Health Study is a prospective National Institutes of Health–sponsored study of adults who were age ≥ 65 years at baseline in 1989–1990.[17] An additional African American cohort of 687 persons with measurements of pulmonary function and other risk factors was enrolled in the period from 1992 to 1993, bringing the total cohort to 5888 persons. Participants in the study were recruited from 4 US geographic regions: Sacramento County, California; Washington County, Maryland; Forsyth County, North Carolina; and Pittsburgh, Pennsylvania. Pulmonary-function test data were available at the baseline examination. Pulmonary-function testing, which includes FVC and FEV_1, was measured with a water-sealed Collins II spirometer (W.E. Collins, Braintree, MA). Details of quality control and missing data due to unreproducible spirometry tests were previously introduced.[18] We also calculated the percent of predicted values using NHANES III reference values.[19] Clinical examinations consisted of assessment of medical history, physical examination, and fasting blood analyses. Seated blood pressure (BP) was measured using the auscultatory method, having the mid-height of the cuff at heart level with the average of 2 measures used. Antihypertensive and lipid treatment data were collected using medication inventory and coded as yes/no in our study.[20] Alcohol intake was measured as number of alcoholic beverages per week; smoking status was categorized as never smoker, former smoker, and current smoker; and high-sensitivity C-reactive protein measures were also available. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation: (LDL-C = total cholesterol – high-density lipoprotein cholesterol [HDL-C] – (1/5) triglycerides [TG]) for TG <400 mg/dL.

Of this sample, we included 4114 participants without a prior history of CVD. Subjects included in the study were stratified by the presence of either DM or MetS. MetS was identified as having any 3 of the following 5 conditions: elevated BP (≥130 mm Hg systolic or ≥ 85 mm Hg diastolic), low HDL-C (<40 mg/dL in males or < 50 mg/dL in females), elevated TG (≥150 mg/dL), increased waist circumference (>88 cm in females or > 102 cm in males), or impaired fasting glucose (IFG; 100–125 mg/dL). DM was defined as having 1 of the following conditions: baseline glucose ≥126 mg/dL after a 12-hour fast, use of oral hypoglycemic agents, or the use of insulin. Participants were categorized as having MetS in our study only if they did not also have DM.

Incident CVD was defined as having stroke, myocardial infarction (MI), heart failure, coronary artery angioplasty, coronary artery bypass surgery, claudication, or angina. Incident coronary heart disease (CHD) was identified as the first occurrence of any of the following: angina, MI, coronary artery angioplasty, coronary artery bypass surgery, or death caused by "atherosclerotic CHD." We also examined the individual CVD components of stroke and congestive heart failure (CHF) as secondary endpoints. Self-report of physician-diagnosed CHF was followed by confirmatory review of the participant's medical records. The presence of CHF was determined from both the diagnosis of CHF by a physician and treatment of CHF (ie, a current prescription for a diuretic agent and either digitalis or a vasodilator). In addition, symptoms, signs, and chest x-ray findings of CHF were reviewed by the CHS Events Committee. The follow-up time was measured from the baseline pulmonary-function testing to date of first occurrence of 1 of the CVD events. The CHS events committee adjudicated all primary CHD and CVD events during the follow-up. Follow-up for events was available through June 2014.

2.1 | Statistical analysis

CHD and CVD events per 1000 person-years, by percent of predicted FEV_1 and FVC quartiles, were calculated and displayed with bar charts. We used multivariate Cox proportional hazards regression to determine hazard ratios (HRs) for CHD and CVD events, adjusted for age, sex, ethnicity, and other non-MetS risk factors, for quartiles of FVC and FEV_1 within MetS and DM, with the lowest quartile as the reference category. In our Cox regression analyses that treated FEV_1 and FVC as continuous markers, FEV_1 and FVC were rescaled by their respective SDs to make direct comparison of HR for 1-SD change of FEV_1 and 1-SD change of FVC. We used C-statistics for survival data to examine whether FVC or FEV_1 add incremental predictive value over risk factors for events in subjects with and without MetS and DM. The statistical procedures were done using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, NC).

3 | RESULTS

Participants were followed for incident CHD and CVD events over a mean follow-up of 12.9 ±4.9 years. Out of the 4241 CVD-free subjects at baseline, 127 did not have lung-function data. They showed slightly higher systolic BP (141 mm Hg vs 136 mm Hg) and higher body mass index (28.0 kg/m^2 vs 26.5 kg/m^2) than those included, but other risk factors were similar. The remaining 4114 participants were included in the study; 1277 (31.0%) had MetS and 537 (13.1%) had DM. Among those with neither MetS nor DM, 24.3% had central obesity (waist circumference > 102 cm for male and > 88 for female), 8.0% had low HDL-C (<40 mg/dL for male and < 50 mg/dL for female), 9.2% had elevated TG (≥150 mg/dL), 58.1% had elevated BP (≥130 mm Hg systolic or ≥ 85 mm Hg diastolic), and 29.1% had IFG

(100–125 mg/dL). Among those with MetS but no DM, 76.0% had central obesity (waist circumference > 102 cm for male and > 88 for female), 50.8% had low HDL-C (<40 mg/dL for male and < 50 mg/dL for female), 58.8% had elevated TG (≥150 mg/dL), 88.3% had elevated BP (≥130 mm Hg systolic or ≥ 85 mm Hg diastolic), and 77.3% had IFG (100–125 mg/dL). Individuals with MetS and DM had significantly lower HDL-C values and significantly higher C-reactive protein and systolic and diastolic BP than participants with neither condition. The cumulative incidences of CVD (64.6% and 54.9% vs 45.9%; $P < 0.001$), CHD (41.9% and 35.7% vs 28.7%; $P < 0.001$), CHF (34.6% and 28.3% vs 22.0%; $P < 0.001$), and stroke (23.3% and 17.5% vs 15.5%) were higher among those with DM and MetS, respectively, than those with neither condition. Individuals with MetS had higher total cholesterol and LDL-C values than did those with DM. Furthermore, those with MetS and DM had poorer lung function than did those with neither disease. FEV_1 for those with IFG was higher than that of those with DM (2.1 L vs 2.0 L, and 87% vs 84% for percent predicted FEV_1, both $P < 0.05$); FVC was comparable between those with IFG and those with DM. The baseline characteristics for the study population can be found in Table 1.

Analyses of CVD incidence per 1000 person-years show that the lowest quartiles of percent predicted FEV_1 and FVC have the highest risks for CVD, compared with the highest quartiles (Figure 1). Within each quartile, CVD incidence was noticeably higher among individuals with MetS and was also higher among individuals with DM compared with those with no DM/MetS.

Comparing the fourth vs first quartiles for FVC, the risk of CVD events was lower by 16% (HR: 0.84, 95% CI: 0.59–1.18), 23% (HR: 0.77, 95% CI: 0.60–0.99), and 30% (HR: 0.70, 0.58–0.84), respectively, in the DM, MetS, and neither disease groups; for FEV_1, CVD risk was lower by 2.0% (HR: 0.98, 95% CI: 0.70–1.37), 26% (HR: 0.74, 95% CI: 0.59–0.93), and 31% (HR: 0.69, 95% CI: 0.57–0.82) in DM, respectively (Table 2). Individuals with DM and MetS had attenuated associations of FEV_1 and FVC with CHD and CVD events vs those with neither disease. Persons with DM had weaker associations between the pulmonary variables and CHD and CVD events than did those with or without MetS, except for heart failure (HF), which had strong associations with both FEV_1 and FVC in all disease groups. No significant relationship was observed between FEV_1 or FVC and stroke. Among 1656

TABLE 1 Means and proportions across disease groups in the Cardiovascular Health Study

	Overall, N = 4114	Neither, n = 2300 (55.9%)	MetS, n = 1277 (31.0%)	DM, n = 537 (13.1%)	*P* Value
Demographics					
Mean age, y	72.4 ± 5.4	72.5 ±5.6	72.1 ±5.0	72.7 ±5.5	0.04
Male sex	1603 (39.0)	9356 (40.7)	418 (32.7)	250 (46.6)	0.0001
Race					
Caucasian	3581 (87.0)	2021 (87.9)	1140 (89.3)	420 (78.2)	0.0001
African American	507 (12.3)	267 (11.6)	129 (10.1)	111 (20.7)	0.0001
Risk factors					
FEV_1, L	2.07 ±0.66	2.12 ±0.68	2.00 ±0.62	2.00 ±0.67	0.0001
% of predicted FEV_1	88.5 ±21.8	90.3 ±21.9	86.9 ±21.4	84.7 ±21.4	0.0001
FVC, L	2.13 ±0.69	2.18 ±0.71	2.05 ±0.64	2.10 ±0.70	0.0001
% of predicted FVC	68.2 ±18.7	69.4 ±18.4	66.8 ±18.4	66.4 ±19.8	0.0001
TC, mg/dL	212.7 ±38.8	211.5 ±36.6	217.7 ±40.3	205.8 ±42.6	0.0001
HDL-C, mg/dL	55.8 ±15.7	61.1 ±15.6	49.1 ±13.0	48.7 ±12.7	0.0001
LDL-C, mg/dL	129.9 ± 35.5	128.0 ±33.8	135.1 ±36.8	125.5 ±38.0	0.0001
SBP, mm Hg	136.0 ±21.3	132.5 ±21.3	140.1 ±19.8	141.4 ±21.6	0.0001
DBP, mm Hg	71.1 ±11.2	70.2 ±11.2	72.3 ±10.7	72.1 ±11.8	0.0001
Current smoker	493 (12.0)	286 (12.4)	148 (11.6)	59 (11.0)	0.57
BMI, kg/m^2	26.5 ±4.54	24.8 ±3.74	28.7 ±4.49	28.5 ±4.73	0.0001
Glucose, mg/dL	108.5 ±32.78	96.4 ±8.52	105.2 ±9.02	168.6 ±58.94	0.0001
Family history of CVD	1391 (33.81)	748 (32.52)	452 (35.40)	191 (35.57)	0.14
Medications					
HTN medication	1580 (38.41)	618 (26.87)	669 (52.39)	293 (54.56)	0.0001
Lipid-lowering medication	179 (4.35)	81 (3.52)	68 (5.32)	30 (5.59)	0.013
Incident disease					
CVD	2104 (51.1)	1056 (45.9)	701 (54.9)	347 (64.6)	0.0001
CHD	1340 (32.6)	659 (28.7)	456 (35.7)	225 (41.9)	0.0001
CHF	1054 (25.6)	507 (22.0)	456 (28.3)	186 (34.6)	0.0001
Stroke	705 (17.1)	356 (15.5)	224 (17.5)	126 (23.3)	0.0001

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CHF, congestive heart failure; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; FEV_1, 1-second forced expiratory volume; FVC, forced vital capacity; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol. Data are presented as n (%) or mean ± SD.

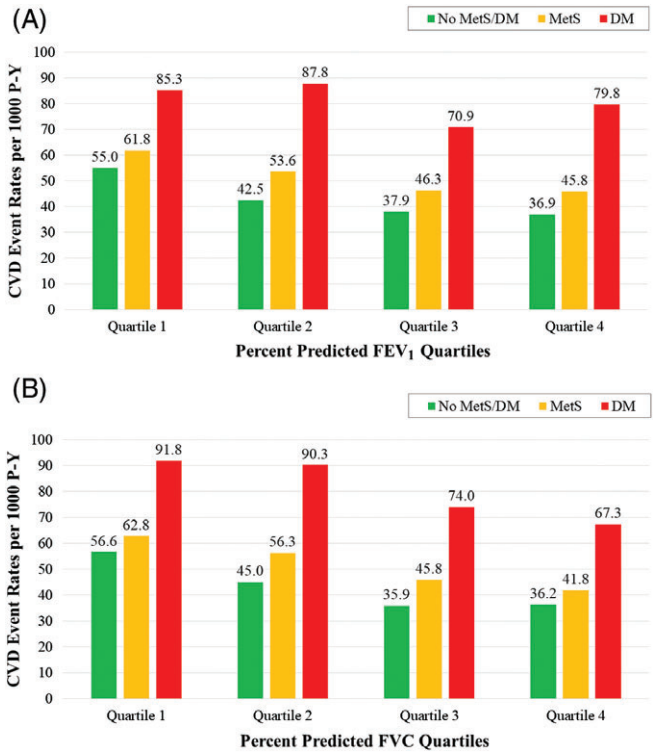

FIGURE 1 Incident CVD event rates per 1000 P-Y by quartile of (A) FEV_1 or (B) FVC. Abbreviations: CVD, cardiovascular disease; DM, diabetes mellitus; FEV_1, 1-second forced expiratory volume; FVC, forced vital capacity; MetS, metabolic syndrome; P-Y, person-years

subjects with IFG, the HR of CVD is 0.92 (0.84–1.00, $P = 0.059$) per 1 SD of FEV_1 and 0.92 (0.84–1.01, $P = 0.079$) per 1 SD of FVC; for CHD, corresponding HRs are 1.01 (0.90–1.13, $P = 0.858$) and 1.02 (0.91–1.14, $P = 0.77$).

We further examined the possible heterogeneous association of lung function and CVD by sex. Females had 22% lower risks of CVD per 1 SD of percent predicted FEV_1 ($P < 0.0001$) and males had a 21% lower risk ($P = 0.0006$); interaction tests for sex and percent predicted FEV_1 were not significant overall as well as in each disease group (interaction test $P = 0.977$, 0.334, 0.922, and 0.134 for overall, no MetS/DM, MetS, and DM groups). For percent predicted FVC, the interaction with sex was also not significant (interaction test $P = 0.763$, 0.502, 0.746, and 0.641 for overall, no MetS/DM, MetS, and DM groups).

C-statistics with only risk factors in the model (Model 1) ranged from 0.611 to 0.658 among the 3 disease groups for CVD events; models with FEV_1 or FVC (Model 2) had a significant increase of C-statistics for CVD events overall and among those with neither disease. For CHD events, C-statistics of Model 1 and Model 2 remain largely unchanged. For incident CHF, C-statistics of Model 1 were generally higher than those for other event types (range, 0.647–0.682 for 3 disease groups); and when FEV_1 or FVC were added, there was significant improvement in C-statistics overall and among those with neither disease (Table 3). Given that FVC and FEV_1 were not associated with stroke (Table 2), C-statistics comparing the 2 models would be no different.

4 | DISCUSSION

The main finding of our study is that among our sample of older adults, higher levels of lung function as measured by FVC and FEV_1 were generally related to lower risks of incident CVD, especially for HF. These results are consistent with those shown in previous studies with broader age-range cohorts.[15,16,21] Although in our study reduced lung function contributed little to CVD risk in DM, recent studies show that reduced lung function may be a precursor of DM.[8] Also, people with reduced lung function have greater levels of inflammation,[22] and people with DM or MetS,[10] including those with elevated C-reactive protein,[23] are at increased risk of CVD. However, the inverse relationships between FEV_1 and FVC with CVD were strongest in those with MetS and no disease, and for CHF held in all 3 disease groups. Although these findings were independent of age, sex, and standard CVD risk factors, added incremental prediction over risk factors was mainly limited to CVD and especially CHF in those with neither disease and was not consistently seen in those with MetS or DM. It is possible that the higher burden of disease in those with DM may make it more difficult to show added prognostic value of other measures, such as lung function. This was also the case where we previously showed left ventricular mass not to add to further prediction of CVD outcomes in Cardiovascular Health Study participants with DM.[24]

Prior studies have been reported on lung function and outcomes in DM or MetS. FEV_1 and FVC have an inverse relationship with type 2 DM and fatal CHD events.[25] In our previous study using NHANES III data with nonsmoking adults ranging in age from 18 to 79 years, we have shown that those with MetS but not DM had increased risk of overall mortality among those with FVC ≤85% predicted, compared with those with FVC ≥95% predicted.[12] Moreover, a smaller community-based sample of older persons with MetS and DM showed MetS and abdominal obesity, but not DM, to be independently associated with restrictive lung disease.[26] Also, although HF risk as a consequence of poor lung function has not previously been reported in MetS and DM patients, others have reported on increased mortality associated with chronic obstructive pulmonary disease (COPD) or restrictive spirometry pattern in patients with HF.[27]

Additionally, other Cardiovascular Health Study investigations have demonstrated the association of smoking with impaired FEV_1/pulmonary function and increased risk of atherosclerosis in the elderly[28,29]; however, other Cardiovascular Health Study studies showed a small association of reduced FEV_1 and FVC with increased risk of CHD outcomes after excluding cigarette smokers and those with lung diseases known to reduce lung function.[30] In our prior NHANES III study, lower FVC did not add to risk of overall mortality among those with only DM[12]; in our current study, higher FVC or FEV_1 was related to lower risk of CHD in those with DM and HF in those with MetS, but not stroke in either condition. Overall, findings between pulmonary function and CHF appeared to be stronger than for other CVD endpoints. This strong relationship between CHF and reduced lung function may be expected, because chronic elevation of atrial pressure due to reduced compliance of left ventricular function is known to cause of elevation of pulmonary artery pressure, which in

TABLE 2 Adjusted Cox proportional hazards regression and 95% CIs for CVD, CHD, CHF, and stroke according to percentage predicted FEV_1 and FVC[a]

	Overall, N = 4036, HR (95% CI)	*P* Value	Neither, n = 2256 (55.9%), HR (95% CI)	*P* Value	MetS, n = 1253 (31.0%), HR (95% CI)	*P* Value	DM, n = 527 (13.1%), HR (95% CI)	*P* Value
CVD								
FEV_1 Q4 vs Q1	0.73 (0.64–0.83)	<0.0001	0.69 (0.57–0.82)	<0.0001	0.74 (0.59–0.93)	<0.05	0.98 (0.70–1.37)	
FVC Q4 vs Q1	0.73 (0.64–0.84)	<0.0001	0.70 (0.58–0.84)	<0.001	0.77 (0.60–0.99)	<0.05	0.84 (0.59–1.18)	
FEV_1 (per SD)	0.88 (0.84–0.93)	<0.0001	0.87 (0.81–0.93)	<0.0001	0.89 (0.82–0.97)	<0.01	0.96 (0.86–1.08)	
FVC (per SD)	0.89 (0.84–0.93)	<0.0001	0.87 (0.81–0.93)	<0.0001	0.90 (0.82–0.98)	<0.05	0.99 (0.86–1.12)	
CHD								
FEV_1 Q4 vs Q1	0.81 (0.69–0.95)	<0.05	0.77 (0.61–0.97)	<0.05	0.83 (0.63–1.10)		0.99 (0.66–1.48)	
FVC Q4 vs Q1	0.83 (0.70–0.98)	<0.05	0.76 (0.60–0.96)	<0.05	0.89 (0.66–1.20)		0.96 (0.63–1.46)	
FEV_1 (per SD)	0.93 (0.87–0.98)	<0.05	0.92 (0.85–1.00)		0.93 (0.84–1.04)		0.96 (0.83–1.11)	
FVC (per SD)	0.93 (0.87–0.99	<0.05	0.92 (0.84–1.01)		0.93 (0.83–1.04)		0.97 (0.83–1.13)	
CHF								
FEV_1 Q4 vs Q1	0.53 (0.44–0.63)	<0.0001	0.49 (0.38–0.63)	<0.0001	0.59 (0.43–0.83)	<0.01	0.48 (0.29–0.78)	<0.01
FVC Q4 vs Q1	0.53 (0.44–0.64)	<0.0001	0.52 (0.40–0.68)	<0.0001	0.53 (0.37–0.76)	<0.001	0.46 (0.28–0.74)	<0.01
FEV_1 (per SD)	0.78 (0.73–0.83)	<0.0001	0.76 (0.69–0.83)	<0.0001	0.80 (0.71–0.90)	<0.001	0.80 (0.69–0.94)	<0.01
FVC (per SD)	0.78 (0.73–0.84)	<0.0001	0.76 (0.69–0.84)	<0.0001	0.80 (0.70–0.91)	<0.001	0.82 (0.70–0.96)	<0.05
Stroke								
FEV_1 Q4 vs Q1	0.89 (0.71–1.11)		0.82 (0.61–1.12)		0.94 (0.63–1.40)		1.17 (0.65–2.10)	
FVC Q4 vs Q1	0.92 (0.73–1.16)		0.97 (0.70–1.33)		0.94 (0.61–1.44)		0.85 (0.47–1.54)	
FEV_1 (per SD)	0.95 (0.86–1.03)		0.94 (0.84–1.05)		0.96 (0.82–1.11)		1.05 (0.86–1.29)	
FVC (per SD)	0.97 (0.89–1.06)		0.95 (0.84–1.07)		0.99 (0.84–1.16)		1.09 (0.88–1.34)	

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CHF, congestive heart failure; CI, confidence interval; CRP, C-reactive protein; CVD, cardiovascular disease; DM, diabetes mellitus; FEV_1, 1-second forced expiratory volume; FVC, forced vital capacity; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; Q, quartile; SBP, systolic blood pressure; SD, standard deviation.

[a] Adjusted for age, sex, race, HTN medication, lipid-lowering medication, alcohol intake, physical activity, education, smoking status, SBP, BMI, family history of CVD, LDL-C, HDL-C, CRP, and glucose level.

turn leads to a reduction of FEV_1 and FVC; however, no significant relationships were found with stroke. In receiver operating characteristic analyses, however, neither FEV_1 nor FVC tended to improve prediction for CVD events over risk factors in MetS or DM. Thus, the utility of FEV_1 and FVC measures to improve risk prediction beyond standard risk factors appears limited in those with MetS and DM.

4.1 | Study limitations

There are several strengths and limitations to our study. The large sample size of the Cardiovascular Health Study provides a sufficient number of CHD and CVD mortality endpoints and adds high power to our study in predicting such outcomes. In addition, the well-standardized measurements of pulmonary function and cardiovascular risk factors were an important contributing strength. The older cohort is a useful population for this topic due to the higher prevalence of MetS, DM, CVD, and pulmonary disease, which are all at increased prevalence. Possible confounding factors were taken into account in the analysis. Nevertheless, the ability of pulmonary-function measures to predict CVD events could be limited by other unmeasured confounders or other comorbidities present in older populations. Previous Cardiovascular Health Study investigations have shown that the most commonly used spirometric reference equations could not create accurate interpretations in the elderly; therefore, some prefer to use actual FVC and FEV_1 measures when examining relationships to risk.[18] Of interest, the Cardiovascular Health Study has shown that older subjects classified as "normal" using the lower limit of normal approach but who have a FEV_1/FVC ratio < 0.70 still have an increased risk of death and COPD-related hospitalization.[31] We only utilized baseline variables both for lung function as well as disease-group classification. It is likely some participants classified as normal at baseline transitioned to MetS or DM and some classified with MetS at baseline transitioned to DM at follow-up. Moreover, the Cardiovascular Health Study has previously reported that those with COPD at baseline were more likely not to have follow-up spirometry tests, and those in the most rapidly declining quartile of FEV_1 had a modest increase in risk of hospital admissions and death from COPD.[32] Other potentially important measures, including total lung capacity and residual volume, were also not available in our sample, so we were thus unable to examine them in relation to outcomes.

The primarily Caucasian and African American sample of the Cardiovascular Health Study limits the extrapolation of this study's findings to other ethnic groups. Also, as we had an insufficient proportion of subjects in our sample with restrictive (0.3%) or mixed (0.9%) lung disease to examine prognosis, others have previously reported such subjects also to have increased mortality, suggesting they deserve similar attention as those with an obstructive pattern.[33] Finally, since the baseline Cardiovascular Health Study examination, the use of preventive therapies such as statins and antihypertensive medication has improved dramatically; it is

TABLE 3 C-statistics for disease groups with percent predictive FEV_1 and FVC as added risk factors in predicting events

	Model 1, C-statistic (95% CI)	Model 2	Model 2, C-statistic (95% CI)	*P* Value of Model 1 vs Model 2
CVD events				
Overall, N = 4114	0.658 (0.645–0.671)	With FEV_1	0.661 (0.648–0.674)	0.032
		With FVC	0.661 (0.648–0.674)	0.077
Neither, n = 2300	0.658 (0.641–0.675)	With FEV_1	0.664 (0.647–0.681)	0.002
		With FVC	0.663 (0.646–0.680)	0.003
MetS, n = 1277	0.632 (0.609–0.654)	With FEV_1	0.632 (0.610–0.655)	0.841
		With FVC	0.632 (0.609–0.654)	0.929
DM, n = 537	0.611 (0.576–0.645)	With FEV_1	0.609 (0.573–0.646)	0.720
		With FVC	0.609 (0.572–0.646)	0.731
CHD events				
Overall, N = 4114	0.654 (0.641–0.668)	With FEV_1	0.655 (0.642–0.669)	0.251
		With FVC	0.655 (0.642–0.669)	0.350
Neither, n = 2300	0.658 (0.638–0.678)	With FEV_1	0.659 (0.639–0.680)	0.418
		With FVC	0.659 (0.639–0.680)	0.441
MetS, n = 1277	0.629 (0.601–0.656)	With FEV_1	0.629 (0.602–0.656)	0.847
		With FVC	0.629 (0.602–0.656)	0.710
DM, n = 537	0.606 (0.570–0.643)	With FEV_1	0.607 (0.570–0.644)	0.829
		With FVC	0.607 (0.570–0.643)	0.992
CHF events				
Overall, N = 4114	0.689 (0.669–0.708)	With FEV_1	0.700 (0.682–0.717)	0.0003
		With FVC	0.698 (0.680–0.716)	0.002
Neither, n = 2300	0.678 (0.653–0.704)	With FEV_1	0.695 (0.671–0.720)	0.0008
		With FVC	0.694 (0.669–0.718)	0.0008
MetS, n = 1277	0.680 (0.652–0.709)	With FEV_1	0.686 (0.656–0.715)	0.328
		With FVC	0.685 (0.655–0.714)	0.404
DM, n = 537	0.649 (0.607–0.690)	With FEV_1	0.656 (0.618–0.694)	0.468
		With FVC	0.652 (0.613–0.690)	0.732

Abbreviations: CHD, coronary heart disease; CHF, congestive heart failure; CI, confidence interval; CVD, cardiovascular disease; DM, diabetes mellitus; FEV_1, 1-second forced expiratory volume; FVC, forced vital capacity; MetS, metabolic syndrome. Model 1 adjusted for age, sex, race, hypertension medication, lipid-lowering medication, alcohol intake, physical activity, education, smoking status, SBP, BMI, family history of CVD, LDL-C, HDL-C, CRP, and glucose level.

possible that relationships we observe between lung-function measures and CVD outcomes may be different if the study were repeated using a more contemporary and better-treated population.

5 | CONCLUSION

Our study supports the use of pulmonary function as an independent predictor of CVD events among our older adult cohort; however, relationships tended to be weaker in those with DM, except for predicting CHF. The predictive ability of pulmonary-function measures over traditional risk factors, however, is limited mainly to those without MetS nor DM, potentially due to the higher burden of risk factors seen in those with MetS and DM.

Conflicts of interest

The authors declare no potential conflicts of interest.

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How to cite this article: Lee HM, Zhao Y, Liu MA, et al. Impact of lung-function measures on cardiovascular disease events in older adults with metabolic syndrome and diabetes. *Clin Cardiol*. 2018;41:959–965. https://doi.org/10.1002/clc.22985