Percent Emphysema and Right Ventricular Structure and Function

The Multi-Ethnic Study of Atherosclerosis-Lung and Multi-Ethnic Study of Atherosclerosis-Right Ventricle Studies

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Background: Severe COPD can lead to cor pulmonale and emphysema and is associated with impaired left ventricular (LV) filling. We evaluated whether emphysema and airflow obstruction would be associated with changes in right ventricular (RV) structure and function and whether these associations would differ by smoking status.

Methods: The Multi-Ethnic Study of Atherosclerosis (MESA) performed cardiac MRI on 5,098 participants without clinical cardiovascular disease aged 45 to 84 years. RV and emphysema measures were available for 4,188 participants. Percent emphysema was defined as the percentage of voxels below -910 Hounsfield units in the lung windows on cardiac CT scans. Generalized additive models were used to control for confounders and adjust for respective LV parameters.

Results: Participants consisted of 13% current smokers, 36% former smokers, and 52% never smokers. Percent emphysema was inversely associated with RV end-diastolic volume, stroke volume, cardiac output, and mass prior to adjustment for LV measures. After adjustment for LV end-diastolic volume, greater percent emphysema was associated with greater RV end-diastolic volume ($+1.5$ mL, $P = .03$) among current smokers, smaller RV end-diastolic volume (-0.8 mL, $P = .02$) among former smokers, and similar changes among never smokers.

Conclusions: Percent emphysema was associated with smaller RV volumes and lower mass. The relationship of emphysema to cardiac function is complex but likely involves increased pulmonary vascular resistance, predominantly with reduced cardiac output, pulmonary hyperinflation, and accelerated cardiopulmonary aging.

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Abbreviations: LV = left ventricular; MESA = Multi-Ethnic Study of Atherosclerosis; RV = right ventricular

Chronic lower respiratory disease, which encompasses emphysema and COPD, is the third-leading cause of death in the United States.¹ Emphysema is characterized by the destruction of alveolar walls and the permanent enlargement of air spaces distal to the terminal bronchioles.² COPD is defined by a reduction in the FEV₁/FVC ratio that is incompletely reversible to bronchodilators.³

COPD is characterized by increased pulmonary artery pressure either at rest or with exercise.^{4,5} A subset of patients with COPD have increased pulmonary arteriovenous pressure gradient, right ventricular (RV) enlargement (termed cor pulmonale), and RV

failure, classically in association with gas trapping and bronchitis.^{5,6} Other (and currently most) patients with very severe COPD do not develop cor pulmonale or RV failure but still have reduced cardiac output. This latter group classically has emphysema.⁷

Although the RV changes in response to severe lung disease are reasonably well described, the impact of milder and subclinical emphysema and airflow obstruction on the right ventricle is less clear. We observed previously that emphysema on CT scan and airflow obstruction on spirometry were associated with significant decrements in left ventricular (LV) filling, stroke volume, and cardiac output, particularly in cigarette

smokers, in a large, population-based study.⁸ Whether these changes are accompanied by an increase in pulmonary arteriovenous pressure gradient with increased RV volumes and mass or, alternatively, reduced cardiac output with reduced RV dimensions is unknown.

We, therefore, examined the relationships between the percent emphysema on CT scan and airflow obstruction on spirometry and RV structure and function on MRI in a large population-based cohort. We first examined associations of lung measures with the right ventricle unadjusted for LV measures. We then evaluated associations of lung measures and the right ventricle adjusted for LV measures because an increased pulmonary arteriovenous pressure gradient should exert a differential effect on the right ventricle and the left ventricle. We used two-tailed *P* values to provide a valid statistical test of either possibility. Given prior findings of effect modification of emphysema-LV associations by smoking status,⁸ we tested for similar effect modification for the right ventricle.

MATERIAL AND METHODS

Study Participants

The Multi-Ethnic Study of Atherosclerosis (MESA) is a multicenter, prospective cohort study of the prevalence, correlates, and

progression of subclinical cardiovascular diseases in whites, blacks, Hispanics, and Asians.⁹ Between 2000 and 2002, MESA recruited 6,814 participants who were 45 to 84 years of age, did not report clinical cardiovascular disease, weighed <136 kg (300 lb), and had no impediment to long-term participation. Written informed consent was obtained from all participants. The protocols of MESA were approved by the institutional review boards of all collaborating institutions and by the National Heart, Lung, and Blood Institute (e-Appendix 1).

Measurements of RV Structure and Function

The MESA-Right Ventricle Study measured RV morphology in 4,204 MESA participants with interpretable cardiac MRIs at the baseline examination (Fig 1). The protocol, its reliability, and the characteristics of MESA participants with MRI measurements have been described previously (e-Appendix 2).¹⁰

Assessment of Emphysema

The MESA-Lung Study quantitatively assessed the extent of emphysema on the lung fields of all baseline MESA cardiac CT scans, which included approximately 70% of the lung volume from the carina to the lung bases. Cardiac CT scans were obtained at full inspiration on multidetector and electron-beam CT scanners according to a standardized protocol.¹¹ Two scans were obtained for each participant, and the scan with the greater volume of lung air was used for analyses, except in cases of discordant scan quality, when the higher-quality scan was analyzed (e-Appendix 2).¹²

Spirometry

The MESA Lung Study performed spirometry between 2004 and 2006 in a subset of MESA participants. Spirometry was performed in accordance with the American Thoracic Society-European Respiratory Society recommended guidelines¹³ (e-Appendix 2).

Smoking Status and Other Covariates

Age, sex, race or ethnic group, educational level, cigarettes smoked per day, number of pack-years of smoking, and medical history were self-reported. Height, weight, resting BP, serum glucose level, C-reactive protein level, and fibrinogen level were measured using standard techniques.¹⁴ A history of hypertension or diabetes and the use of insulin or hypoglycemic or anti-hypertensive agents were determined. Study participants who reported having smoked at least one cigarette in the 30 days before the CT scan examination or who had a urinary cotinine level >100 ng/mL on the day of the CT scan examination were classified as current smokers.

Statistical Analysis

The data are presented as the mean $\pm$ SD for continuous variables and as percentages for discrete variables for all participants and are stratified by smoking status. Effect modification of the relationship of pulmonary measures with RV measures by smoking status was anticipated *a priori*⁸ and was tested with the -2 log-likelihood test of nested models with and without interaction terms.

We used generalized additive models to regress RV end-diastolic volume, stroke volume, ejection fraction, and mass on percent emphysema stratified by smoking status and on the FEV₁/FVC ratio. The first model was adjusted for age, race or ethnicity, sex, height and weight, cigarettes smoked per day, number of pack-years of smoking, serum glucose, diabetes, systolic and diastolic

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FIGURE 1. Flow diagram of participant selection in the MESA study. LV = left ventricular; MESA = Multi-Ethnic Study of Atherosclerosis; RV = right ventricular.

BP, hypertension, educational attainment, serum glucose level, C-reactive protein level, and fibrinogen level. Analysis of percent emphysema was further adjusted for CT scanner type and tube current in milliamperes, which affect attenuation. Corresponding LV parameters were then added (except for stroke volume because of the interrelatedness of the variables).

Sensitivity analyses were conducted using percent emphysema in lung cores, peels, and upper-lobe regions as independent variables, stratifying by pack-years of smoking instead of smoking status and in the subsample of individuals with no restrictive ventilatory defect on spirometry. The test of the primary hypothesis, 95% CIs, and *P* values were estimated from generalized additive models. A two-tailed *P* value < .05 was considered to indicate statistical significance. Analyses were performed using R statistical software, version 2.13.0 (R Foundation for Statistical Computing).

RESULTS

Of the 6,814 MESA participants, 5,098 underwent cardiac MRI examination, of whom 5,004 had interpretable LV measures; 4,634 were selected for RV interpretation, and 4,204 were completed (Fig 1). Three were missing CT scans, and 13 were missing information on covariates, resulting in a sample size

of 4,188 with percent emphysema measures. Spirometric measures were available for 2,741.

The mean age of the study sample was 61 years, and 47% were men (Table 1, e-Table 1). One-half were never smokers, 36% had smoked in the past, and 13% were current smokers. Mean spirometric measurements and RV parameters are shown in Table 2 and e-Table 2. The median value for percent emphysema was 18.4%.

Emphysema and RV Function

Percent emphysema was inversely associated with RV end-diastolic volume, stroke volume, cardiac output, and mass in the main multivariable models (all *P* < .001). However, there were significant interactions between RV end-diastolic volume and smoking status and percent emphysema (*P* = .012 for interaction); hence, analyses for percent emphysema were stratified by smoking status.

Greater percent emphysema was associated with smaller RV end-diastolic volume after adjustment for covariates in current, former, and never smokers (Table 3). The magnitude of this association was greater among current and former smokers compared

Table 1—Characteristics of Participants With Right Ventricular Measures in the Multi-Ethnic Study of Atherosclerosis Study Stratified by Smoking Status

Characteristic	Smoking Status		
	Current Smokers (n = 528, 13%)	Former Smokers (n = 1,494, 36%)	Never Smokers (n = 2,166, 52%)
Age, y	58 ± 9	63 ± 10	61 ± 10
Male	280 (53)	871 (58)	837 (39)
Race/ethnicity			
White	183 (35)	716 (48)	742 (34)
Black	196 (37)	385 (26)	521 (24)
Hispanic	128 (24)	292 (20)	504 (23)
Asian	21 (4)	101 (7)	399 (18)
Educational attainment			
No high school degree	99 (19)	198 (13)	385 (18)
High school degree	111 (21)	264 (18)	404 (19)
Some college	258 (49)	731 (49)	958 (44)
Greater than bachelor's degree	60 (11)	301 (20)	419 (19)
Height, cm	168 ± 9	169 ± 9	164 ± 10
Weight, kg	79 ± 16	80 ± 16	75 ± 16
BMI, kg/m ²	27.7 ± 4.8	28.1 ± 4.9	27.8 ± 5.1
Body surface area, m ²	1.9 ± 0.2	1.9 ± 0.2	1.8 ± 0.2
Pack-y of smoking ^a	22 (9-38)	13 (4-29)	...
Hypertension (physician diagnosis or treatments)	199 (38)	742 (50)	944 (46)
Systolic BP	123 ± 21	126 ± 21	126 ± 21
Diastolic BP	72 ± 10	72 ± 10	71 ± 10
Diabetes mellitus (physician diagnosis or treatments)	57 (11)	181 (12)	249 (12)
Fasting plasma glucose, mg/dL	95 (89-104)	96 (89-105)	96 (90-105)
C-reactive protein, mg/L	2.7 (1.1-4.8)	1.7 (0.7-4.0)	1.7 (0.8-3.9)
Fibrinogen, mg/100 mL	348 (302-400)	330 (288-377)	340 (297-388)
Asthma (physician diagnosis)	45 (9)	144 (10)	204 (9)
Emphysema or chronic bronchitis (physician diagnosis)	38 (12)	102 (10)	89 (6)
Airflow limitation	107 (34)	261 (28)	235 (16)

Data are presented as No. (%), median (IQR), or mean ± SD. IQR = interquartile range.

^aIn ever smokers.

with never smokers. Generalized additive models did not reveal a nonlinear component of the relationships (Fig 2).

Greater percent emphysema was also associated with smaller RV stroke volume, irrespective of smoking status, and lower RV mass in adjusted models

(Table 3). These findings were statistically significant, except for RV mass among current smokers. Percent emphysema was inversely associated with cardiac output among never smokers, but there was no evidence of an association with RV ejection fraction or cardiac output in current smokers.

Table 2—Percent Emphysema on CT Scan, Lung Function, and RV Structure and Function on MRI Stratified by Smoking Status

Lung and RV Parameters	Current Smokers (n = 528)	Former Smokers (n = 1,494)	Never Smokers (n = 2,166)
Percent emphysema, median (IQR)	13.4 (6.8-23.7)	22.1 (13.0-32.7)	17.0 (8.5-27.2)
FEV ₁ , ^a % predicted	85.2 ± 17.6	94.1 ± 18.3	96.8 ± 16.3
FVC, ^a % predicted	91.5 ± 16.1	97.1 ± 16.5	96.7 ± 15.4
FEV ₁ /FVC ratio, ^a %	72.0 ± 10.8	73.5 ± 8.9	76.6 ± 7.2
RV mass, g	21.7 ± 4.5	21.6 ± 4.5	20.6 ± 4.4
RV end-diastolic volume, mL	126.9 ± 30.2	128.7 ± 31.2	120.3 ± 30.2
RV stroke volume, mL	87.5 ± 20.0	89.8 ± 21.1	84.6 ± 20.0
RV cardiac output, L/min	5.5 ± 1.6	5.7 ± 1.7	5.5 ± 1.6
RV ejection fraction, %	69.4 ± 6.7	70.2 ± 6.3	70.9 ± 6.5
Body surface area corrected measures			
RV mass, g/m ²	11.5 ± 1.9	11.3 ± 1.9	11.3 ± 1.9
RV end-diastolic volume, mL/m ²	67.2 ± 12.7	67.5 ± 13.0	65.9 ± 12.4
RV stroke volume, mL/m ²	46.4 ± 8.8	47.2 ± 9.2	46.5 ± 8.5

Data are presented as mean ± SD unless indicated otherwise. RV = right ventricular. See Table 1 legend for expansion of other abbreviations.

^an = 313, 951, and 1,485 for current, former, and never smokers, respectively.

Table 3—Mean Differences in RV Parameters per 10 Percentage-Point Change in Percent Emphysema According to Smoking Status in Multivariable Models

RV Parameter	Current Smokers (n = 528)		Former Smokers (n = 1,494)		Never Smokers (n = 2,166)	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
RV end-diastolic volume, mL	−2.43 (−4.16 to −0.70)	.006	−3.25 (−4.20 to −2.29)	< .001	−1.38 (−2.17 to −0.59)	< .001
RV stroke volume, mL	−1.53 (−2.80 to −0.25)	.019	−1.83 (−2.55 to −1.12)	< .001	−1.10 (−1.69 to −0.52)	< .001
RV cardiac output, L/min	0.00 (−0.10 to 0.11)	.934	−0.04 (−0.11 to 0.02)	.190	−0.13 (−0.18 to −0.08)	< .001
RV ejection fraction, %	+0.06 (−0.47 to +0.58)	.838	+0.28 (+0.03 to +0.54)	.030	−0.14 (−0.38 to 0.09)	.233
RV mass, g	−0.26 (−0.53 to +0.01)	.059	−0.43 (−0.57 to −0.29)	< .001	−0.19 (−0.31 to −0.06)	.004

Adjusted for age, weight, height, sex, race/ethnicity, cigarettes per day (current smokers only), pack-y of smoking (current and former smokers only), glucose, diabetes (physician diagnosis or treatment), systolic and diastolic BP, hypertension (physician diagnosis or treatment), educational attainment, fibrinogen, and C-reactive protein, and CT scanner type and tube current in milliamperes. See Table 2 legend for expansion of abbreviations.

After additional adjustment for respective LV measures, greater percent emphysema was associated with larger RV end-diastolic volume and greater RV cardiac output among current smokers (Fig 3, Table 4). Among former smokers, percent emphysema was associated with smaller RV end-diastolic volume and greater RV cardiac output after adjustment for LV measures. Among never smokers, there was no evidence of an association between percent emphysema and RV end-diastolic volume or RV cardiac output after adjustment for LV measures. Greater percent emphysema was also weakly associated with RV ejection fraction in former smokers and with lower RV mass among former and never smokers after adjustment for respective LV measures (Table 4).

Airflow Obstruction and RV Function

There was no evidence of interactions between RV parameters and spirometry by smoking status; therefore, these analyses were not stratified by smoking status (Table 5). Lower FEV₁/FVC ratio was associated with lower RV mass after adjustment for LV mass. There were no other associations between FEV₁/FVC ratio and RV parameters (Table 5, e-Table 3).

Additional Analyses

There was no evidence of effect modification by sex, race or ethnic group, or obesity (all $P > .23$ for interaction). Associations between percent emphysema and RV measures were similar when percent emphysema in lung core, peel, and upper-lobe regions were used as independent variables (e-Tables 4-6). Effect modification by smoking history was also present (eg, $P = .021$ for RV end-diastolic volume), and results stratified by pack-years of smoking yielded results similar to those stratified by smoking status (e-Fig 1, e-Table 7). Results were similar when a -950 threshold was used to define percent emphysema (e-Table 8) and when we considered individuals with no restrictive ventilatory defect on spirometry (e-Table 9).

DISCUSSION

Percent emphysema was inversely associated with RV end-diastolic volume, stroke volume, and mass, independent of major confounders in this large, population-based cohort free of clinical cardiovascular disease. Associations varied according to smoking status and were of greater magnitude among ever smokers compared with never smokers. Relative to previously observed decrements in LV volumes and mass, percent emphysema was associated with higher RV end-diastolic volume and RV cardiac output in current smokers, lower RV end-diastolic volume in former smokers, and similar decrements in RV and LV end-diastolic volumes in never smokers.

These findings, along with the previously reported large decrement in LV end-diastolic volume with emphysema,⁸ suggest that greater percent emphysema may lead to reduced filling of the right ventricle and reduced cardiac output (with reduced pulmonary blood flow). In fact, there was indirect evidence of increased RV afterload only among current smokers (ie, large RV end-diastolic volume and greater RV cardiac output relative to LV parameters, the latter presumably due to regurgitant flow into the low-pressure vena cava), which was mild (ie, no accompanying increase in RV mass). The underlying mechanisms of these findings may include destruction of the pulmonary vascular bed in emphysema related to apoptosis of the pulmonary endothelium,^{15,16} endothelial dysfunction¹⁷ or hypercoagulability,¹⁸ a reduction in pulmonary blood flow and LV cardiac output, and an increase in pulmonary vascular resistance.

In addition, there may be a direct effect of hyperinflation and unloading of both ventricles, particularly among never and former smokers.^{19,20} Hyperinflation of the lungs has two principal causes: hyperexpansion of the chest due to emphysema-related loss of elastic recoil and increased intrathoracic pressure (ie, intrinsic positive end-expiratory pressure) due to gas trapping and airflow obstruction. Hyperexpansion due to loss of elastic recoil may reduce venous return to the

Current smokers

Former smokers

Never smokers

FIGURE 2. Relationship between RV end-diastolic volume and % emphysema across smoking categories. Models were adjusted for age, weight, height, sex, race/ethnicity, CT scanner type and tube current in milliamperes, cigarettes per day (only current smokers), pack-y of smoking (only current and former smokers), glucose, diabetes (physician diagnosis or treatment), systolic and diastolic

right ventricle and left ventricle because of cardiac rotation and distortions in the systemic and pulmonary vascular structure, respectively. Hyperinflation and gas trapping due to intrinsic positive end-expiratory pressure may impair cardiac filling by reduced venous return to the thorax¹⁹ and by direct compression of the heart and pulmonary vessels,²¹ increasing end-diastolic stiffness of the right ventricle and increasing pulmonary arteriovenous pressure gradients, as has been suggested previously in moderate-severe COPD.^{19,20} Although intrathoracic pressure was not measured (and was infeasible) in this large epidemiologic study, the former mechanism (hyperinflation and gas trapping) appears a more likely explanation for our findings in most of the sample, given that associations were predominantly observed with percent emphysema rather than airflow obstruction.²²

Reduced LV preload due to chronic thromboembolic pulmonary hypertension causes a reduction in LV mass and ventricular atrophy.²³ Our observations could also be consistent with a similar off-loading of the right ventricle from reduced systemic venous return from emphysema-related hyperinflation.

Among current smokers, percent emphysema was positively associated with greater RV end-diastolic volume and less of a reduction in RV cardiac output after adjustment for LV end-diastolic volume. This finding suggests that increased RV afterload in early, mostly subclinical, emphysema occurs predominantly in current smokers.

Alternatively, biologic aging contributes to lung function decline (approximately 20–25 mL/y in nonsmokers) and to alterations in LV and RV structure and function.^{24,25} It is well known that emphysema occurs with age, in addition to occurring with smoking. In addition, percent emphysema was associated with decreasing LV volumes in never smokers.⁸ Therefore, the links between radiologic emphysema and RV morphology may also reflect biologic aging.

Study Limitations

This study has several potential limitations. Smoking may be an important confounder, and former smokers had higher percent emphysema than did current smokers. Previous studies have shown similar results,^{8,22,26–27} likely because inflammatory cell infiltration and mucus from current smoking make the lung appear denser (ie, lower percent emphysema). To address this limitation, we adjusted all analyses for cigarettes smoked per day. In addition, we performed sensitivity analyses controlling for cotinine level (in the

BP, hypertension (physician diagnosis or treatment), educational attainment, fibrinogen, and C-reactive protein. See Figure 1 legend for expansion of abbreviations.

Table 4—Mean Differences in RV Parameters per 10 Percentage-Point Change in Percent Emphysema According to Smoking Status in Multivariable Models After Adjustment for Respective LV Parameters

RV Parameter	Current Smokers (n = 528)		Former Smokers (n = 1,494)		Never Smokers (n = 2,166)	
	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value	Coefficient (95% CI)	P Value
RV end-diastolic volume, mL	+1.50 (+0.15 to +2.84)	.030	−0.83 (−1.56 to −0.13)	.021	+0.03 (−0.54 to +0.59)	.928
RV stroke volume, mL	+0.88 (−0.07 to +1.83)	.071	−0.03 (−0.54 to +0.48)	.915	+0.09 (−0.32 to +0.51)	.656
RV cardiac output	+0.08 (+0.02 to +0.15)	.008	+0.04 (0.00 to +0.08)	.039	+0.01 (−0.02 to +0.04)	.462
RV ejection fraction, %	−0.09 (−0.58 to +0.40)	.716	+0.30 (+0.06 to +0.53)	.013	−0.07 (−0.28 to +0.15)	.535
RV mass, g	−0.17 (−0.42 to +0.09)	.179	−0.32 (−0.45 to −0.18)	<.001	−0.16 (−0.27 to −0.04)	.010

Adjusted for age, weight, height, sex, race/ethnicity, cigarettes per day (current smokers only), pack-y of smoking (current and former smokers only), glucose, diabetes (physician diagnosis or treatment), systolic and diastolic BP, hypertension (physician diagnosis or treatment), educational attainment, fibrinogen, and C-reactive protein, and CT scanner type and tube current in milliamperes, and respective LV parameters. LV = left ventricular. See Table 2 legend for expansion of other abbreviations.

large subset with cotinine measures) and excluding current smokers, which yielded similar results.

Given the limited number of current smokers and the relatively modest smoking exposure among former smokers, we were unable to differentiate effect modification from smoking status from that due to cumulative smoking history. Current smoking was precisely assessed by cotinine levels; the multivariate results changed little with adjustment for multiple measures of smoking (data not shown), and percent emphysema was associated with RV parameters even among never smokers.

Percent emphysema was measured only on partial-lung rather than full-lung CT scans; however, MESA cardiac scans image approximately 70% of the lung volume in the field of view, and percent emphysema measures from these scans correlate with full-lung measures ($r = 0.93$).¹² The upper lobes are classically involved in smoking-related centrilobular emphysema, and a recent study showed that upper-lobe-predominant emphysema was significantly associated with greater lung function decline in former and current heavy smokers.²⁸ However, cardiac scans assess lower and central regions of the lung, which receive the greatest amount of pulmonary blood flow in the upright position.^{29,30} Finally, the sensitivity analysis considering the emphysema in the region of the upper lobes included yielded similar results.

Lung function was measured in a subsample approximately 4 years after the other measures. The reduced sample size limited power in this analysis. In addition, we did not measure diffusing capacity for carbon monoxide, which has been associated with more CT scan-quantified emphysema and could refine the COPD phenotype.^{31,32}

Selection bias may affect any cross-sectional study, but is likely to be modest in magnitude in this study because it was population based and participants were not selected on the basis of the presence or absence of lung disease or symptoms. In addition, this design cannot establish temporality. Measurement of right

and left atrial volumes, and hypoxemia and pulmonary artery pressures were not available.

CONCLUSIONS

In conclusion, percent emphysema was inversely associated with RV end-diastolic volume, stroke volume, and mass, independent of major confounders in this large, population-based cohort. Associations differed from those observed for the left ventricle and varied according to smoking status and severity, which suggests that several potential mechanisms underlie cardiopulmonary interactions in a community-based population.

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Current smokers

Former smokers

Never smokers

FIGURE 3. Relationship between RV end-diastolic volume and % emphysema across smoking categories after adjustment for respective left ventricular parameters. Models were adjusted for age, weight, height, sex, race/ethnicity, CT scanner type and tube current in milliamperes, left ventricular end-diastolic volume, cigarettes per day (only current smokers), pack-y of smoking

Table 5—Mean Differences in RV Parameters per 1 Percentage-Point Change in the FEV₁/FVC Ratio (n = 2,741)

RV Parameter	Coefficient (95% CI)	P Value
Model 1 ^a : prior to adjustment of LV parameters		
RV end-diastolic volume, mL	+6.82 (−4.65 to +18.31)	.244
RV stroke volume, mL	+7.57 (−0.91 to +16.05)	.080
RV cardiac output, L/min	−0.18 (−0.96 to +0.59)	.647
RV ejection fraction, %	+2.25 (−1.02 to 5.51)	.178
RV mass, g	+1.29 (−0.43 to +3.01)	.143
Model 2 ^b : after adjustment for LV parameters		
RV end-diastolic volume, mL	+5.44 (−2.74 to +13.62)	.193
RV ejection fraction, %	+1.16 (−1.81 to +4.13)	.444
RV mass, g	+1.89 (+0.26 to +3.52)	.023

See Table 2 and 4 legends for expansion of abbreviations.

^aModel 1 adjusted for age, weight, height, sex, race/ethnicity, cigarettes per day (current smokers only), pack-y of smoking (current and former smokers only), glucose, diabetes (physician diagnosis or treatment), systolic and diastolic BP, hypertension (physician diagnosis or treatment), educational attainment, fibrinogen, and C-reactive protein, and CT scanner type and tube current in milliamperes.

^bModel 2: Model 1 + LV measures.

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Dr Kawut: contributed to the study concept and design; data acquisition, analysis, and interpretation; critical revision of the manuscript for intellectual content; and final approval of the submitted manuscript.

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Additional information: The e-Appendix and e-Tables can be found in the “Supplemental Materials” area of the online article.

(only current and former smokers), glucose, diabetes (physician diagnosis or treatment), systolic and diastolic BP, hypertension (physician diagnosis or treatment), educational attainment, fibrinogen, and C-reactive protein. See Figure 1 legend for expansion of abbreviations.

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