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Pulmonary Hyperinflation and Left Ventricular Mass

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Abstract

Background—Left ventricular (LV) mass is an important predictor of heart failure and cardiovascular mortality, yet determinants of LV mass are incompletely understood. Pulmonary hyperinflation in chronic obstructive pulmonary disease (COPD) may contribute to changes in intrathoracic pressure that increase LV wall stress. We therefore hypothesized that residual lung volume in COPD would be associated with greater LV mass.

Methods and results—The Multi-Ethnic Study of Atherosclerosis (MESA) COPD Study recruited smokers aged 50–79 years who were free of clinical cardiovascular disease. LV mass was measured by cardiac magnetic resonance. Pulmonary function testing was performed according to guidelines. Regression models were used to adjust for age, sex, body size, blood pressure and other cardiac risk factors.

Among 119 MESA COPD Study participants, mean age was 69±6 years, 55% were male and 65% had COPD, mostly of mild or moderate severity. Mean LV mass was 128±34 grams. Residual lung volume was independently associated with greater LV mass (7.2 grams per standard deviation increase in residual volume; 95% CI 2.2 to 12; P=0.004), and was similar in magnitude to that of systolic blood pressure (7.6 grams per standard deviation increase in systolic blood pressure, 95% CI 4.3 to 11 grams; p<0.001). Similar results were observed for LV mass to end-diastolic volume ratio (p=0.02) and with hyperinflation measured as residual volume to total lung capacity ratio (P=0.009).

Conclusions—Pulmonary hyperinflation, as measured by residual lung volume or residual lung volume to total lung capacity ratio, is associated with greater LV mass.

Keywords

Left ventricular mass; hyperinflation; chronic obstructive pulmonary disease

INTRODUCTION

Heart disease and chronic obstructive pulmonary disease (COPD) are leading causes of mortality in the United States.[1] These two common diseases often co-exist: for example, approximately 35% of patients hospitalized for heart failure have COPD when tested systematically, and clinical or subclinical cardiovascular disease is increased in COPD independent of shared risk factors.[2-4] The physiologic mechanisms underlying this association remain incompletely understood.

Left ventricular (LV) mass predicts incident cardiovascular events, including heart failure, sudden death and cardiovascular mortality,[5-7] and regression of LV mass from afterload reducing therapies is associated with improved cardiovascular outcomes.[8-10] Early autopsy and ventriculography studies reported increased LV mass and wall thickness in the presence of obstructive lung disease,[11-13] subsequent studies, however, produced conflicting results and none assessed the role of pulmonary hyperinflation.[14-18]

COPD is a heterogeneous disorder defined by persistent airflow limitation that arises from increased airways resistance (e.g., airway narrowing) and loss of lung elastic recoil (e.g.,

emphysema).[19-20] Pulmonary hyperinflation occurs in COPD and other obstructive lung diseases due in part to impaired expiratory airflow.[19, 21] Breathing at the resultant increased lung volume requires more negative inspiratory pleural pressure, the magnitude of which can be large (e.g., 4-10 mmHg at rest and 13-16 mmHg on exercise).[22-26] On expiration, airway pressures in obstructive lung disease increase, but to a lesser extent when compared to inspiration (e.g., 1.6 to 3.2 mmHg).[23-24] Indeed, a study of reversible airways obstruction demonstrated mean pleural pressure over the entire respiratory cycle to be more negative during exacerbation (−16 mmHg in exacerbation versus −5 mmHg in controls).[26] Inspiratory maneuvers generating negative pleural pressure have been shown to alter juxtacardiac pressure resulting in increased LV transmural pressure load which augments LV wall stress.[27-31] Although it is well-known that chronic exposure to increased LV wall stress results in LV hypertrophy,[32] studies assessing the relationship of pulmonary hyperinflation to LV mass are lacking.

We hypothesized that residual lung volume, a standard clinical measure of hyperinflation on body plethysmography,[19] would be independently associated with greater LV mass on cardiac magnetic resonance (MR) in COPD.

METHODS

Study participants

The multicenter Multi-Ethnic Study of Atherosclerosis (MESA) COPD Study recruited unmatched cases of COPD and controls from MESA, a population-based prospective cohort study of subclinical atherosclerosis,[33] and the Emphysema and Cancer Action Project (EMCAP),[34] a separate, non-overlapping lung cancer screening study, in addition to a small number from the local outpatient community. Included participants were 50–79 years of age with ≥10 pack-year smoking history. Exclusion criteria were clinical cardiovascular disease (physician diagnosis of myocardial infarction, angina, heart failure, valve disease, atrial fibrillation or stroke), stage IIIb-V chronic kidney disease, asthma prior to age 45 years, prior lung resection, cancer, allergy to gadolinium, claustrophobia, metal in the body and pregnancy. The current report describes the 119 participants recruited from EMCAP and the outpatient community at one site, Columbia University Medical Center, for whom body plethysmography was performed. Ninety of these participants were recruited from EMCAP and 29 from the local outpatient community (Figure 1), the latter via flyers and local physicians.

Pulmonary Function Testing

Body plethysmography and post-bronchodilator spirometry were assessed using a V6200 Series Autobox (Sensormedics, Yorba Linda, CA) and an OMI rolling barrel spirometer following American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations[35-36] and as previously described.[37] Functional residual capacity was measured while panting at a frequency of 0.5–1.0 Hz. At least 2 technically satisfactory maneuvers were performed, followed by a linked inspiratory capacity maneuver, and slow vital capacity maneuver. Functional residual capacity was reported as the mean of the satisfactory measurements. Plethysmographic total lung capacity was calculated as the sum

of functional residual capacity and inspiratory capacity, and residual volume as the difference between total lung capacity and slow vital capacity, and reported in liters at body temperature and pressure saturated. Predicted spirometry values were calculated using Hankinson reference equations,[37] and Garcia-Rio equations for lung volumes for participants 65 years and older and Crapo equations for lung volumes for participants under 65 years.[6-7] COPD status and severity were defined as per ATS/ERS COPD criteria.[38]

Cardiac magnetic resonance (MR) and LV mass analysis

LV mass was assessed by cardiac MR following the MESA Exam 5 protocol. Images were obtained using a 1.5 Tesla whole-body MR system (Signa LX, GE Healthcare). Ventricular structure and function was measured with images in short-axis orientation with 12 or more slices using a retrospectively gated steady state free precession sequence. Imaging parameters were: TR/TE: 5.6/1.7ms, slice thickness: 8mm, gap: 2mm, FOV: 360×360mm, matrix: 256×192. Cine images were reconstructed at 20–35-msec intervals over the cardiac cycle with 40 phases. Semi-automated contouring was used to determine LV mass, volumes and ejection fraction (Cardiac Image Modeller, NZ),[39] in addition to right ventricular parameters using QMass (v7.2, Medis, The Netherlands).[40] LV wall thickness was measured from the inferoseptal and lateral walls of mid-ventricular short-axis cine images at the end-diastolic phase.

Chest computed tomography (CT) and assessment of emphysema

Participants underwent full-lung thoracic CT on a GE 64-slice helical scanner (120 kVp, 200mAs at 0.5 seconds) with 0.75 mm slice thickness. Images were obtained at suspended full inspiration. Image attenuation was assessed at a single reading center by trained readers without knowledge of other participant information (VIDA Diagnostics, Coralville IA). Percent of emphysema-like lung (also known as percent low attenuation area and hereafter referred to as percent emphysema) was defined as the percentage of total voxels within the lung field which fell below −950 Hounsfield units (HU).[41]

Anthropometry, blood pressure and other co-variates

Height and weight were measured following the MESA protocol,[42] as was resting seated blood pressure, which was measured 3 times with Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, GE Healthcare, Waukesha, Wisconsin). Age, gender and race or ethnic group were self-reported. Smoking history was assessed using standard questionnaire items and was confirmed with plasma cotinine levels (Immulite 2000 Nicotine Metabolite Assay; Diagnostic Products Corp., Los Angeles, CA, USA). Information on medication use was obtained by medication inventory.[43] Glucose and cholesterol were measured from blood samples after a twelve-hour fast. Hypertension was defined according to the seventh report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure.[44]

Study Oversight

Study procedures were approved by the institutional review boards of the participating institutions and by the National Heart, Lung, and Blood Institute. Written informed consent was obtained from all participants in the MESA COPD Study.

Statistical Analysis

The cohort was stratified by percent predicted residual lung volume for descriptive purposes. Dichotomous variables are presented as proportions and continuous variables as means with standard deviation unless otherwise indicated. Bivariate comparisons were tested by Chi-square, Fisher's exact or Student t-tests where appropriate. Simple linear regression was performed for crude comparisons between LV mass and measures of pulmonary hyperinflation.

The primary analysis of the relationship between LV mass and residual volume was performed using multiple linear regression with adjustment for the following potential confounders: age, gender, height, body size indexing term and race-ethnicity. The body size indexing term is similar to body surface area but specific to LV mass and was included as a co-variate.[45] A second model adjusted for additional potential confounders including current smoking status, systolic blood pressure, hypertension, diabetes, total cholesterol level and lipid lowering medication use. Percent emphysema and the forced expiratory volume in the first second (FEV_1) were also included in the second model, given that emphysema on CT scan has associated with reduced LV mass,[46] and the contribution of reduced lung elastic recoil to impaired airflow,[20] respectively. To minimize the possibility of confounding by body size, we repeated analyses for a second measure of hyperinflation, residual volume to total lung capacity ratio. A generalized additive model with locally weighted smoothing function was used to test for non-linearity of the relationship between residual volume and LV mass.

As recruitment in this largely nested case-control study was based on COPD status (presence/absence), ignoring the sampling strategy would yield non-conservative standard errors for the association of two continuous measures, hyperinflation and LV mass.[47] In an effort to obtain unbiased, population-based effect estimates, participants were weighted on the inverse ratio of probability of selection. Weights were computed as the ratio of case or control prevalence in the source study population to that in the MESA COPD Study. In primary analyses, participants recruited from the local community were assigned the same weights as those recruited from EMCAP. Sensitivity analyses were performed without any sample weighting, restricting the sample to participants from the EMCAP cohort only, using an additional term for participant recruitment source and with alternate weighting for those recruited from the local community based on the National Health and Nutrition Examination Survey III.[48] We chose a conservative analysis method in which standard errors were computed by first summing empirical estimates of the covariance matrices of COPD-stratum specific contributions to the gradient of the weighted sum of squares, and pre- and post-multiplying by the matrices of mixed partial derivatives of the gradient weighted sum of squares evaluated at the weighted least squares solutions (analogous to generalized estimated equation estimator).[47] Analyses were stratified by hypertension and COPD status,

were restricted to participants without physician diagnosed obstructive sleep apnea, diabetes, bronchodilator use, systolic ejection fraction ≤50 percent or current smoking status, were performed without terms for percent emphysema and FEV_1 in the model. Additional sensitivity analyses included terms for educational attainment, fasting plasma glucose, right ventricular mass, right ventricular enddiastolic volume, oxygen saturation, and using alternate metrics of body size, smoking intensity, percent emphysema and lipid profile.

RESULTS

Pulmonary Hyperinflation and LV Mass

Potential participants from EMCAP and the community who were screened and enrolled are shown in the Figure 1. EMCAP participants who were not enrolled into the MESA COPD Study were more obese, had greater number of pack-years of smoking and differed by race-ethnicity compared to those in the analysis (Supplementary Appendix Table S1). Participants enrolled in the MESA COPD Study who did not complete cardiac MR or plethysmography were more obese, with higher blood pressure, lower lung function, and fewer years of formal education (Supplementary Appendix Table S2).

Of the 119 participants who completed plethysmography and cardiac MR, the mean age was 69±6 years, 55% were male and the mean LV mass was 128±34 grams. Table 1 summarizes the characteristics of the study participants stratified by quartile of percent predicted residual lung volume. Seventy-seven (65%) of participants had COPD, mostly of mild or moderate severity. Mean age, percent male and body size were approximately equal across quartiles but the prevalence of current smoking, hypertension and diabetes increased. Severity of COPD, alternate measures of hyperinflation, and percent emphysema also increased with residual lung volume.

A significant association was observed between pulmonary hyperinflation, as measured by residual lung volume, and LV mass (Table 2). In the fully adjusted model, a one standard deviation increase in residual volume (0.71 L) was associated with 7.2 gram increase in LV mass (95% CI 2.2 to 12 grams; p=0.004). By comparison, a one standard deviation increase in systolic blood pressure (16 mmHg) was associated with 7.6 gram increase in LV mass (95%CI 4.3 to 11 grams; p<0.001) in the same model. Figure 2 shows the fully adjusted relationship of residual lung volume to LV mass from a smoothed regression model. There was no evidence for non-linearity (i.e., a threshold effect) in this relationship (p=0.32). The increase in LV mass associated with residual volume was approximately symmetric: residual volume was associated with increases in inferoseptal and lateral wall thickness in fully adjusted models of 0.5 and 0.4 mm, respectively, per SD unit (95% CI 0.1 to 0.8 mm and 0.0 to 0.7 mm; p=0.01 and p=0.03). In addition, residual volume was associated with greater LV mass to end-diastolic volume ratio (Table 2) and there was no evidence of effect modification by gender (p-interaction=0.15).

Residual volume was not associated with right ventricular mass or end-diastolic volume in fully adjusted models (−0.2 gram change in right ventricular mass per SD increase in residual lung volume; 95% CI −1.3 to 0.9 grams; p=0.74; 2.3 mL change in right ventricular end-diastolic volume per SD increase in residual volume; 95% CI −5.0 to 9.6 mL; p=0.54).

Further, the association between residual volume and LV mass remained significant with additional adjustment for right ventricular mass (p=0.004) or end-diastolic volume (p=0.009).

Similar significant associations were observed in fully adjusted models for residual volume to total lung capacity ratio with LV mass and LV mass to end-diastolic volume ratio (Table 2). There were no statistically significant relationships of functional residual capacity or total lung capacity to these cardiac parameters (Supplementary Table S3).

Sensitivity Analyses

Among participants without hypertension a one standard deviation increase in residual volume was associated with 7.2 gram greater LV mass (95%CI 1.9 to 12; p=0.02). The association was also significant in unweighted analyses (8.0 gram increase in LV mass per standard deviation increase in residual volume [95%CI 3.2 to 13 grams; p=0.001]) and among former smokers (10 gram increase in LV mass per standard deviation increase in residual volume [95%CI 5.3 to 15 grams; p<0.001]). Similar results were obtained in sensitivity analyses that used alternate approaches to population weighting, alternate adjustments for body size, smoking intensity, cardiac risk factors, percent emphysema, lung function and resting oxygen saturation, restriction for medication use, obstructive sleep apnea, diabetes and LV ejection fraction (Figure 3). In stratified analyses, the association between pulmonary hyperinflation and LV mass was greater among those with COPD and attenuated among those without COPD (Figure 3), although there was no evidence for effect modification by COPD status (p-interaction=0.84).

DISCUSSION

Pulmonary hyperinflation, as measured by residual lung volume or residual volume to total lung capacity ratio, was associated with greater LV mass independent of blood pressure and other traditional cardiac risk factors among older smokers with predominantly mild-to-moderate COPD. The magnitude of the association of residual volume to LV mass was similar to that of systolic blood pressure.

The current report is the first, to our knowledge, to consider the relationship between pulmonary hyperinflation and LV mass. Our findings, based on pulmonary function testing and cardiac MR, are consistent with early autopsy studies that described LV hypertrophy in patients with chronic obstructive lung disease.[12-13] Similarly, Baum and colleagues demonstrated LV dysfunction and increased LV wall thickness by ventriculography among fifteen patients with very severe obstructive lung disease.[11] Subsequent studies failing to show an association between COPD and LV mass did not account for several known determinants of LV mass or omitted morphologic (i.e. emphysema) and physiologic (i.e. hyperinflation) derangements that often accompany COPD.[14-18]

LV mass predicts incident cardiovascular events.[5, 7] In the present study of predominantly mild-to-moderate COPD, hyperinflation was associated with ~5% increase in LV mass per standard deviation increase in residual volume. In prior longitudinal studies, an increase in LV mass of this magnitude was associated with 6% increase in all-cause mortality, 7%

increase in risk of cardiovascular death and 20% increase in risk of incident heart failure.[5, 7] COPD increases risk of sudden death and heart failure.[49-50] Increased LV mass in COPD might contribute in part to this risk, although this hypothesis was not tested directly in the present study. Measures of hyperinflation were also associated with LV mass to end-diastolic volume ratio. This metric of concentric LV remodelling also predicts incident cardiovascular events and is associated with heart failure with preserved ejection fraction,[51] a condition frequently associated with COPD.[2]

Changes in pleural pressure influence juxtacardiac pressure.[30] Further, it has been shown that more negative pleural pressures increase LV transmural pressure, effectively augmenting LV wall stress.[27-29] The resulting increase in stroke work may represent a mechanism by which hyperinflation is associated with increased LV mass. In support of this proposed mechanism, prior studies have demonstrated that patients with COPD and hyperinflation generate more negative pleural pressure on inspiration during tidal volume breathing (e.g., 4-10 mmHg at rest and 13-16 mmHg on exercise).[22-24] Applied over time and greater on exertion, these pressure changes may explain the greater LV mass observed with hyperinflation.

Advanced COPD is associated with right ventricular dysfunction which may have impacted on LV structure or function via mechanisms of cardiac chamber interdependence.[52] In the present study, however, measures of hyperinflation were not associated with right ventricular mass or end-diastolic volume. Further, additional adjustment for right ventricular dimensions did not alter the association between hyperinflation and LV mass. Conceivably, a mechanism by which hyperinflation increases atrial dimensions could also lead to greater LV chamber diameter and thus, LV wall stress. While the atria were not fully imaged in this study, prior work by Watz and colleagues has shown hyperinflation to be associated with reduced atrial and ventricular chamber dimensions.[53] We therefore believe that mechanisms involving cardiac chamber interdependence are less likely to explain the observed association between hyperinflation and LV mass.

Hyperinflation can be defined various ways, but generally refers to an increase in residual volume, functional residual capacity, total lung capacity, or ratios thereof.[19] In COPD, hyperinflation can result from increases in airways resistance (e.g., airway narrowing), lung compliance (e.g., emphysema), or both.[19] In our study, residual volume had the strongest association with LV mass and residual volume to total lung capacity ratio was also associated with LV mass. Functional residual capacity and total lung capacity are thought to be more sensitive to changes in lung elastic recoil from emphysema.[19, 54-55] In the context of our proposed mechanism of greater negative inspiratory pressures increasing LV afterload, residual volume may be a better metric of hyperinflation with preserved lung elastic recoil. Coexistent emphysema may attenuate the magnitude of these inspiratory pressure swings by increasing lung compliance.[19, 54-55] Consistent with this framework, emphysema has been shown to be associated with reduced LV mass.[46] Also, residual volume is the first lung volume to increase in COPD.[56-57] In our study of predominantly mild-to-moderate COPD, the range of hyperinflation as measured by functional residual capacity or total lung capacity may have been insufficient to demonstrate an association with LV mass.

The present study has several limitations. First, residual confounding by hypertension or other confounders may have contributed to the observed association. However, restricting our analysis to participants with or without hypertension while adjusting for blood pressure yielded similar results, as did similar analyses for diabetes and smoking status. Second, the proposed mechanism relating hyperinflation to LV mass remains speculative, as we did not directly measure LV transmural pressure or wall stress. The measures to demonstrate such a mechanism are too invasive to be applied to a population-based study of participants free of clinical cardiovascular disease with predominantly mild-to-moderate COPD. Third, we did not formally assess patients for obstructive sleep apnea, which can also generate negative pleural pressure and is associated with increased LV mass.[58-59] However, obstructive sleep apnea is associated with reduced static lung volumes and would therefore be expected to weaken the association observed in this study.[60] Inclusion of self-reported physician diagnosis of obstructive sleep apnea did not alter our observation. Fourth, selection bias can be of concern in MR studies; however, weighting based on the source population COPD prevalence, as well as various other weighting schemes and analyses nested only within EMCAP yielded consistent results. Fifth, the cross-sectional design prevents inference on the direction of the association. On physiological grounds we believe the effect of hyperinflation on LV mass is more likely than the reverse. Sixth, participants that were not enrolled or with incomplete data differed with respect to anthropometrics, smoking history, blood pressure and spirometry when compared to those included in analyses. This may limit the generalizability of our findings despite efforts to obtain population-based effect estimates. Finally, we did not measure dynamic hyperinflation. We suspect, however, that greater intrathoracic pressure changes with dynamic hyperinflation would strengthen the association with LV mass.

In summary, residual lung volume and residual lung volume to total lung capacity ratio were associated with greater LV mass. Pulmonary hyperinflation in obstructive lung disease may represent a novel and modifiable risk factor for cardiovascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Clinical Summary

Heart disease and chronic obstructive pulmonary disease (COPD) are leading causes of mortality in the United States that often co-exist. Left ventricular (LV) mass predicts cardiovascular events including heart failure and mortality, yet determinants of LV mass are incompletely understood. Early physiological studies suggest pulmonary hyperinflation in obstructive lung disease may contribute to changes in intrathoracic pressure that alter juxtacardiac pressure and effectively *increase* LV afterload on inspiration. The relationship of pulmonary hyperinflation to LV mass has never been assessed.

The current study provides evidence, for the first time, that pulmonary hyperinflation is strongly associated with greater LV mass in a population with predominantly mild-to-moderate COPD, independent of blood pressure and other traditional cardiac risk factors. The magnitude of this association was similar to that of systolic blood pressure. Pulmonary hyperinflation was also associated with greater LV mass to end-diastolic volume ratio, suggesting a pattern of concentric remodelling.

In summary, this study identifies a novel relationship between two common and deadly diseases. Further investigation is required to determine if pulmonary hyperinflation in obstructive lung disease may represent a novel and modifiable risk factor for cardiovascular disease.

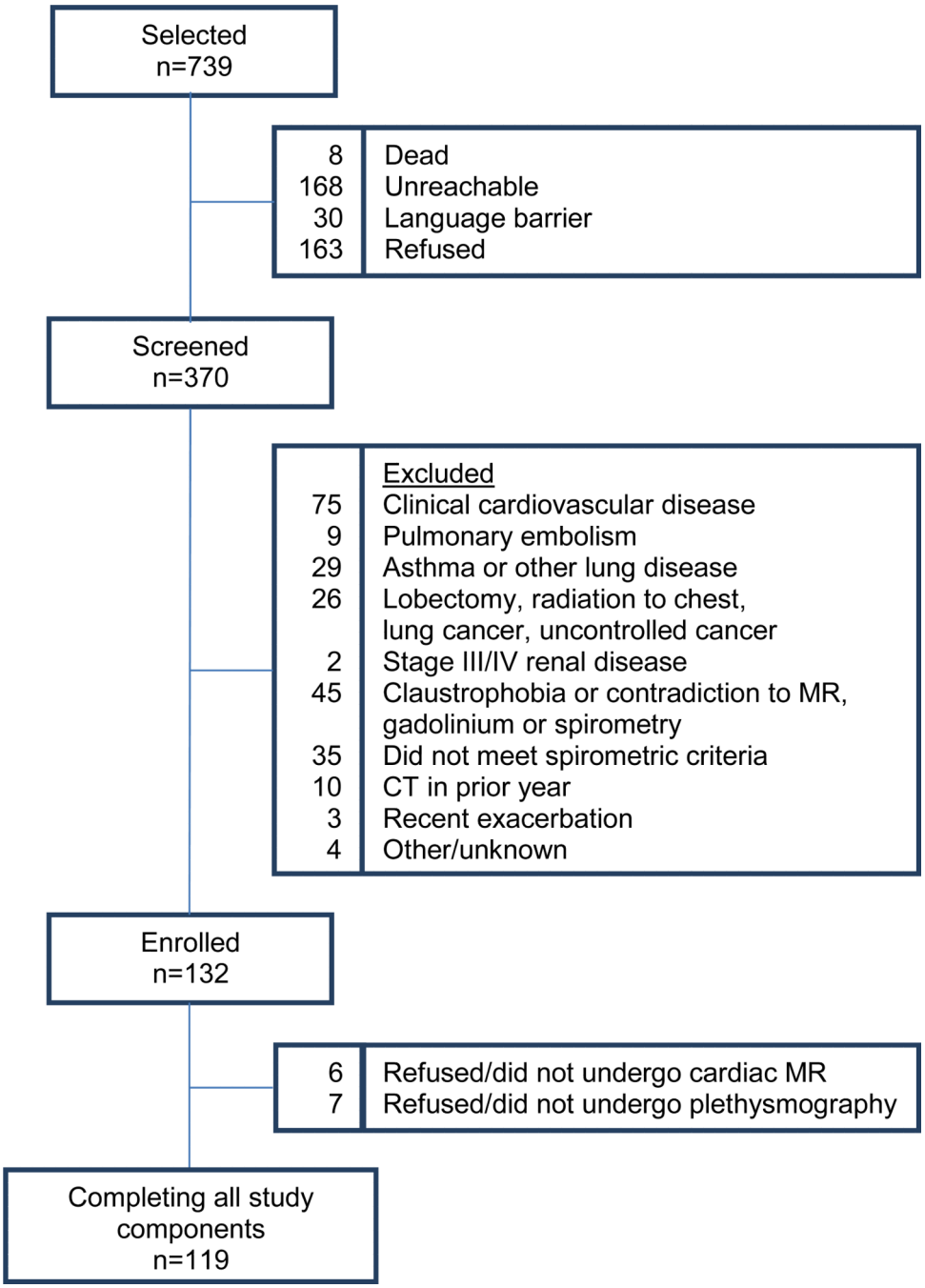

Figure 1.

Flowchart of Study Participants in the LV Mass and Hyperinflation Analysis. Flowchart of screening and enrollment of participants included in the analysis with body plethysmography and cardiac MR. Abbreviations: LV denotes left ventricle, MR magnetic resonance and CT computed tomography.

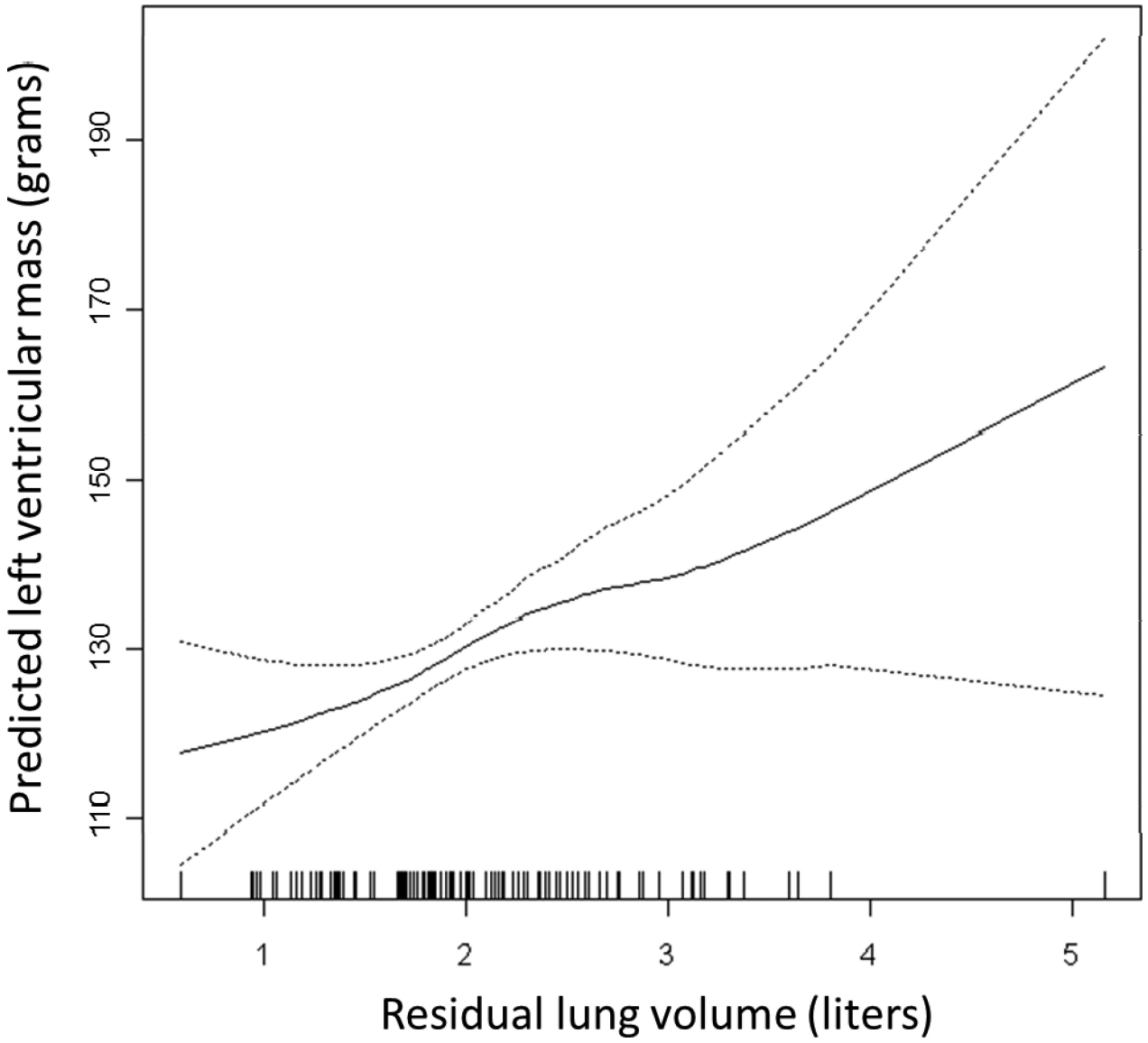

Figure 2.

Relationship Between Residual Lung Volume and Left Ventricle Mass in the MESA COPD Study. Results of a multi-variate analysis of the relationship between residual lung volume and left ventricular mass are shown. Tick marks above the X-axis represent observed residual volume measures. Predicted left ventricular mass is represented by the solid line and was obtained from a smoothed regression model adjusted for age, gender, race or ethnic group, height, body size indexing term[45], systolic blood pressure, hypertension, diabetes, total cholesterol, lipid lowing medication use, current smoking status, FEV_1 and percent $emphysema_{-950\ HU}$. The dashed lines represent the 95% confidence boundary. Abbreviations: HU denotes Hounsfield units, FEV_1 forced expired volume in the first second. Test for non-linearity: p=0.32.

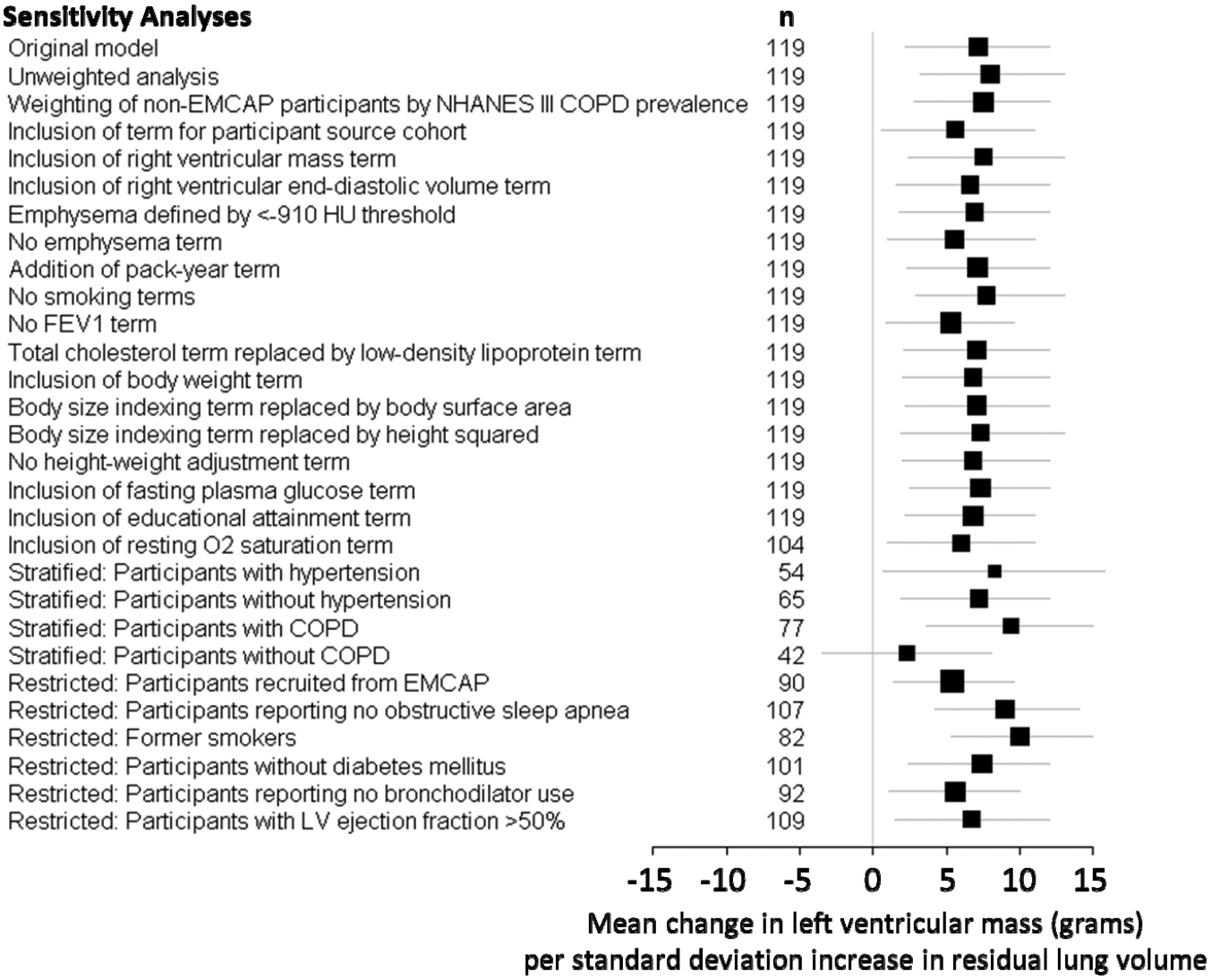

Figure 3.

Mean Increment in Left Ventricle Mass by Residual Lung Volume in the MESA COPD Study. Original model was adjusted for: age, gender, race or ethnic group, height, body size indexing term, systolic blood pressure, hypertension, fasting plasma glucose level, diabetes, total cholesterol, lipid lowing medication use, current smoking status, FEV_1 and percent $emphysema_{-950\ HU}$. Abbreviations: HU denotes Hounsfield units, FEV_1 forced expired volume in the first second, EMCAP Emphysema and Cancer Action Project, NHANES National Health and Nutrition Examination Survey, COPD chronic obstructive pulmonary disease, LV left ventricle and CI confidence interval.

Table 1

Baseline Characteristics of MESA COPD Study Participants Stratified by Quartiles of Percent Predicted Residual Lung Volume.

Characteristic	Quartiles of Percent Predicted Residual Volume			
No.	1.33 L N=29	1.73 L N=30	2.09 L N=30	2.89 L N=30
Age - years	69±5	69±6	69±8	68±6
Male sex - no. (%)	17 (59)	16 (53)	15 (50)	18 (60)
Race or ethnic group - no. (%)†				
Caucasian	19 (66)	23 (77)	24 (80)	23 (77)
African American	5 (17)	4 (13)	5 (17)	7 (23)
Other	5 (17)	3 (10)	1 (3)	0 (0)
Height - cm	169±11	168±9	167±10	169±9
Weight - kg	77±16	79±17	75±18	76±19
Body-surface area - m^2	1.9±0.2	1.9±0.2	1.9±0.3	1.9±0.3
Cigarette smoking status - no. (%)				
Former smoker	21 (72)	18 (60)	20 (67)	15 (50)
Current smoker	8 (28)	12 (40)	10 (33)	15 (50)
Pack-years of smoking - no.†				
Median (IQR)	36 (27)	32 (26)	40 (30)	50 (34)
Blood pressure - mm Hg				
Systolic	119±15	119±16	126±18	123±13
Diastolic	67±9	70±12	72±10	75±9
Hypertension - no. (%)	7 (24)	12 (40)	17 (57)	16 (53)
Fasting plasma glucose - mg/dl				
Median (IQR)	96 (19)	104 (22)	102 (20)	98 (17)
Diabetes mellitus - no. (%)	2 (7)	4 (13)	6 (20)	6 (20)
Total Cholesterol - mg/dl	183±36	197±45	187±41	178±37
Lipid lowering med use - no. (%)	15 (52)	8 (27)	15 (50)	11 (37)
COPD - no. (%)	13 (45)	16 (53)	21 (70)	27 (90)
GOLD - COPD severity - no. (%)				
Mild	9 (31)	7 (23)	11 (37)	2 (7)
Moderate	4 (14)	9 (30)	8 (27)	13 (43)
Severe / very severe	0 (0)	0 (0)	2 (7)	12 (40)
Plethysmography:				
Residual volume - L	1.33±0.30	1.73±0.31	2.09±0.35	2.89±0.64

Characteristic	Quartiles of Percent Predicted Residual Volume			
FRC - L	2.94±0.75	2.99±0.67	3.41±0.71	4.04±0.80
TLC - L	5.28±1.27	5.48±1.18	5.69±1.21	6.14±1.14
Residual volume to TLC ratio	0.26±0.04	0.32±0.04	0.37±0.04	0.47±0.07
Post-bronchodilator spirometry:				
FEV_1 - L	2.54±0.68	2.46±0.64	2.15±0.69	1.54±0.55
FVC - L	3.63±0.97	3.61±0.92	3.47±0.95	3.14±0.86
FEV_1 to FVC ratio	0.70±0.07	0.69±0.09	0.62±0.12	0.50±0.12
Percent emphysema$_{-950\ HU}$ - median (IQR)	1.2 (2.4)	1.4 (2.4)	1.7 (3.9)	7.7 (16)
Left ventricle measures:				
Mass - grams	122±29	131±39	129±34	131±35
End-diastolic volume - ml	121±26	116±26	114±23	112±36
End-systolic volume - ml	49±14	44±15	46±14	46±21
Stroke volume - ml	71±16	72±16	68±14	66±18
Ejection fraction - %	59±6	62±7	60±7	60±8
Mass to end-diastolic volume ratio	1.03±0.18	1.13±0.26	1.13±0.17	1.20±0.22
Inferoseptal wall thickness - mm	9.6±1.7	10±2.1	10±1.7	11±1.9
Lateral wall thickness - mm	7.9±1.4	8.8±1.9	8.9±1.4	8.8±1.5

Plus-minus values are means ± standard deviation.

Abbreviations: COPD denotes chronic obstructive pulmonary disease, GOLD Global Initiative for Chronic Obstructive Lung Disease, FRC functional residual capacity, TLC total lung capacity, FEV1 forced expired volume in the first second, FVC forced vital capacity and HU Hounsfield units.

† Race or ethnic group, smoking status and pack-year history were self-reported.

Table 2

Mean Increment in Left Ventricle Mass According to Measures of Hyperinflation in the MESA COPD Study.

Left Ventricular Mass	Quartiles of residual lung volume				Mean increment in grams of LV mass per standard deviation increase in residual lung volume (95% CI)	P Value
Mean residual volume - L	1.24	1.71	2.15	2.99		
LV mass - grams	109	121	135	148	13 (7.8 to 19)	<0.001
Predicted LV mass - grams						
Model 1	125	128	130	134	4.2 (0.2 to 8.2)	0.035
Model 2	119	123	127	135	7.2 (2.2 to 12)	0.004

Left Ventricular Mass to End-Diastolic Volume Ratio	Quartiles of residual lung volume				Mean increment in LV mass to EDV ratio per standard deviation increase in residual lung volume (95% CI)	P Value
Mean residual volume - L	1.24	1.71	2.15	2.99		
LV mass to end-diastolic volume ratio	1.00	1.09	1.19	1.21	0.06 (0.02 to 0.10)	0.001
Predicted LV mass to end-diastolic volume ratio						
Model 1	1.06	1.10	1.13	1.20	0.06 (0.01 to 0.11)	0.016
Model 2	1.03	1.07	1.11	1.18	0.07 (0.01 to 0.13)	0.021

Left Ventricular Mass	Quartiles of residual volume to total lung capacity ratio				Mean increment in grams of LV mass per standard deviation increase in residual volume to total lung capacity ratio (95% CI)	P Value
Mean residual volume to total lung capacity ratio	0.25	0.32	0.38	0.48		
LV mass - grams	124	126	136	127	2.4 (-3.4 to 8.3)	0.42
Predicted LV mass - grams						
Model 1	125	128	130	133	3.1 (-0.5 to 6.7)	0.087
Model 2	119	124	128	134	5.9 (1.4 to 10)	0.009

Left Ventricular Mass to End-Diastolic Volume Ratio	Quartiles of residual volume to total lung capacity ratio				Mean increment in LV mass to EDV ratio per standard deviation increase in residual volume to total lung capacity ratio (95% CI)	P Value
Mean residual volume to total lung capacity ratio	0.25	0.32	0.38	0.48		
LV mass to end-diastolic volume ratio	1.03	1.13	1.15	1.17	0.05 (0.02 to 0.09)	0.005
Predicted LV mass to end-diastolic volume ratio						
Model 1	1.06	1.10	1.14	1.20	0.05 (0.02 to 0.09)	0.004
Model 2	1.03	1.08	1.12	1.19	0.06 (0.01 to 0.12)	0.013

Model 1 adjusted for: age, gender, race-ethnicity, height and body size indexing term[45].

Model 2 additionally adjusted for: systolic blood pressure, hypertension, diabetes, total cholesterol level, lipid lowering medication use, current smoking status, FEV_1 and percent emphysema–950 HU.

Abbreviations: LV denotes left ventricle, CI confidence interval, EDV end-diastolic volume, HU Hounsfield units, and FEV_1 forced expired volume in the first second.