Not All Measures of Hyperinflation Are Created Equal

Lung Structure and Clinical Correlates of Gas Trapping and Hyperexpansion in COPD: The Multi-Ethnic Study of Atherosclerosis (MESA) COPD Study

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e-FIGURE LEGEND

e-Figure 1. Flowchart of Participants from the EMCAP Study and Community Who Were Selected for Plethysmography in the MESA COPD Study.

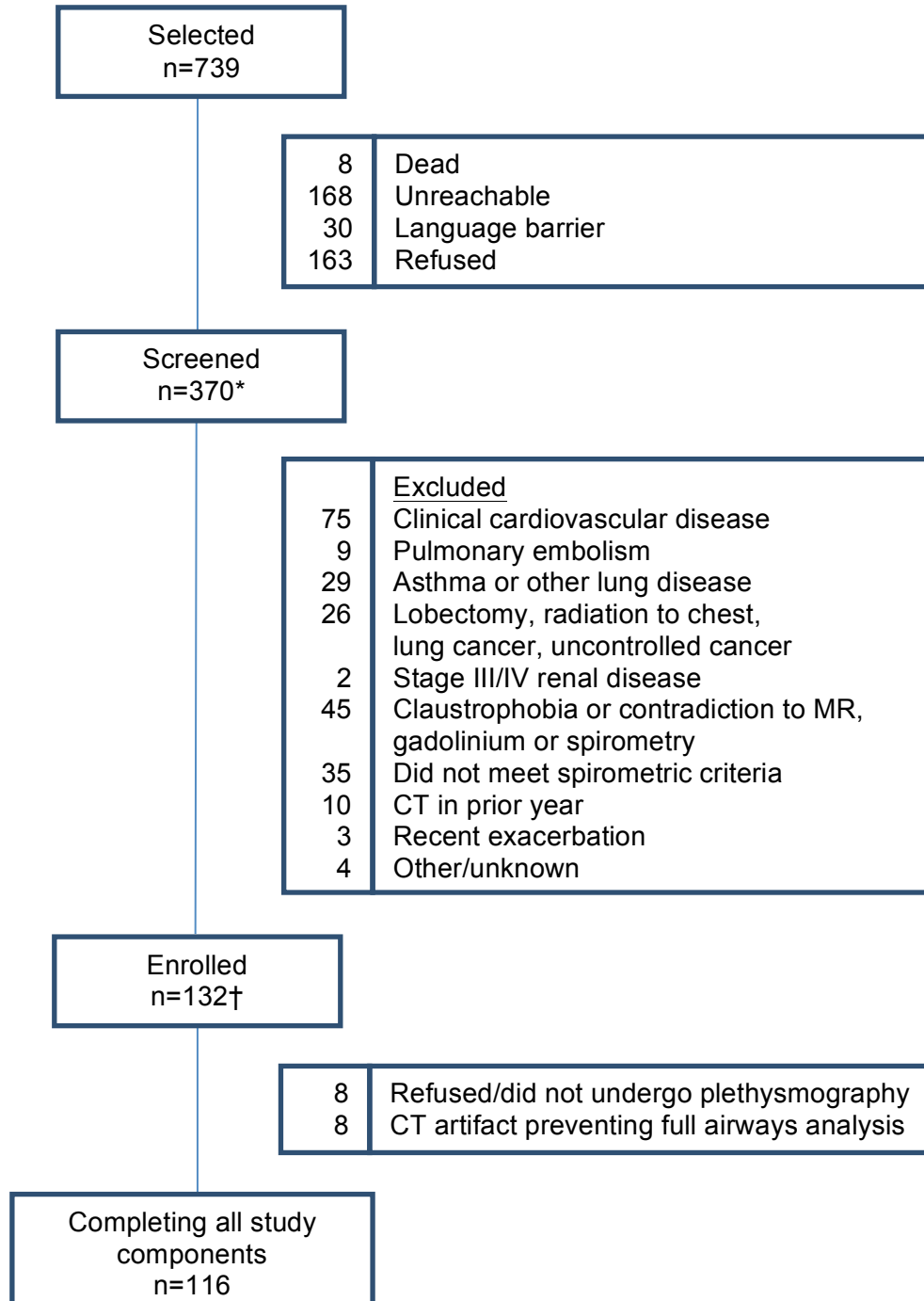*227 participants screened from EMCAP and 143 participants screened from the local community.
†92 participants enrolled from EMCAP and 40 participants enrolled from the local community.

Abbreviations: EMCAP denotes Emphysema and Cancer Action Project, MESA Multi-Ethnic Study of Atherosclerosis, COPD chronic obstructive pulmonary disease, CT computed tomography, and MR magnetic resonance.

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e-Figure 1.

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┌─────────────────┐
│    Selected     │
│     n=739       │
└────────┬────────┘
         │        ┌──────┬──────────────────────────────┐
         │        │   8  │ Dead                         │
         │        │ 168  │ Unreachable                  │
         │        │  30  │ Language barrier             │
         │        │ 163  │ Refused                      │
         │        └──────┴──────────────────────────────┘
┌────────┴────────┐
│    Screened     │
│    n=370*       │
└────────┬────────┘
         │
         │   ┌───────┬──────────────────────────────────────┐
         │   │       │ Excluded                             │
         │   │   75  │ Clinical cardiovascular disease      │
         │   │    9  │ Pulmonary embolism                   │
         │   │   29  │ Asthma or other lung disease         │
         │   │   26  │ Lobectomy, radiation to chest,       │
         │   │       │ lung cancer, uncontrolled cancer     │
         │   │    2  │ Stage III/IV renal disease           │
         │   │   45  │ Claustrophobia or contradiction to MR,│
         │   │       │ gadolinium or spirometry             │
         │   │   35  │ Did not meet spirometric criteria    │
         │   │   10  │ CT in prior year                     │
         │   │    3  │ Recent exacerbation                  │
         │   │    4  │ Other/unknown                        │
         │   └───────┴──────────────────────────────────────┘
┌────────┴────────┐
│    Enrolled     │
│    n=132†       │
└────────┬────────┘
         │   ┌──────┬───────────────────────────────────────┐
         │   │   8  │ Refused/did not undergo plethysmography│
         │   │   8  │ CT artifact preventing full airways analysis│
         │   └──────┴───────────────────────────────────────┘
┌────────┴──────────┐
│ Completing all study│
│     components     │
│      n=116         │
└────────────────────┘
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e-Table 1. Characteristics of Participants Enrolled in the MESA COPD Study with Plethysmography and of EMCAP Participants Selected, Screened but not Enrolled.

Characteristic	MESA COPD Study with Plethysmography* N=132			EMCAP participants screened but not enrolled
	Complete data		Incomplete data	
	from EMCAP	from community		
No.	N=86	N=30	N=16	N=135
Age – years§	71±3	62±5	65±6	71±4
Male sex – %	44	77	44	53
Race or ethnic group – %†				
Caucasian	75	53	69	81
African American	12	47	31	4
Hispanic	7	0	0	12
Asian	6	0	0	2
Education level – %				
Less than high school degree	4	10	6	5
High school degree	22	17	25	16
College degree or more	74	73	69	79
Height – cm	166±10	173±7	168±5	168±9
Weight – kg†	77±21	80±12	80±9	83±17
Body mass index – kg/m^2	28±7	27±3	28±3	29±5
Smoking status – %†				
Former smoker	71	43	69	85
Current smoker	29	57	31	15
Pack-years of smoking – no.†				
Median (1st, 3rd quartile)	36 (24, 52)	37 (25, 53)	43 (33, 54)	47 (29, 62)

Plus-minus values are means ± standard deviation. *Descriptive statistics of enrolled participants weighted by the inverse ratio of probability of selection based on COPD status. †P<0.05 for pair-wise comparison between participants enrolled in the MESA COPD Study and EMCAP participants screened but not enrolled. §P<0.05 for pair-wise comparison between participants enrolled in MESA COPD Study with complete and incomplete data.

Abbreviations: MESA denotes Multi-Ethnic Study of Atherosclerosis, COPD chronic obstructive pulmonary disease, and EMCAP Emphysema and Cancer Action Project.

e-Table 2. Differences in Absolute Lung Volumes and Odds of Absolute Lung Volumes being Above or Below the Limit of Normal by Airway Lumen Diameter with additional adjustment for Percent Emphysema$_{<-950HU}$.

	Predicted difference in lung volume* (95% CI)				
	RV (ml)	**RV/TLC (%)**	**FRC (ml)**	**TLC (ml)**	**IC/TLC (%)**
Per SD decrement in airway lumen diameters	40 ml (10 to 80 ml) P=0.03	0.6% (0.1 to 1.1%) P=0.02	10 ml (-20 to 40 ml) P=0.58	20 ml (-20 to 60 ml) P=0.40	0.0% (-0.5 to 0.5%) P=0.91
	Odds ratios for lung volumes above or below the limit of normal† (95% CI)				
	RV > ULN	**RV/TLC > ULN**	**FRC > ULN**	**TLC > ULN**	**IC/TLC < LLN**
Per SD decrement in airway lumen diameters	1.3 (1.2 to 1.5) P<0.001	1.3 (1.1 to 1.5) P=0.007	0.8 (0.6 to 1.1) P=0.16	1.1 (0.8 to 1.6) P=0.41	1.1 (0.8 to 1.4) P=0.55

Predicted mean differences for the linear term and odds for the dichotomous term were estimated using generalized estimating equations. *Predicted mean differences in lung volumes were adjusted for age, gender, height, weight, body mass index, race or ethnic group, level of education attained, current smoking status, and percent emphysema$_{<-950HU}$. †ULN and LLN were calculated using age, gender, and height-based reference equations, hence logistic models were unadjusted.

Abbreviations: HU denotes Hounsfield units, SD standard deviation, CI confidence interval, RV residual volume, TLC total lung capacity, FRC functional residual capacity, IC inspiratory capacity, ULN upper limit of normal, and LLN lower limit of normal.

e-Table 3. Differences in Absolute Lung Volumes by Airway Wall Thickness and Percent Airway Wall Thickness.

Lung structure metric	Predicted difference in lung volume (95% CI)				
	RV (ml)	RV/TLC (%)	FRC (ml)	TLC (ml)	IC/TLC (%)
Per SD increment in percent airway wall thickness	70 ml (20 to 120 ml) P=0.009	0.9% (0.3 to 1.7%) P=0.007	20 ml (-40 to 80 ml) P=0.53	30 ml (-40 to 100 ml) P=0.44	0.0% (-0.6 to 0.6%) P=0.98
Per SD increment in airway wall thickness	-30 ml (-60 to 10 ml) P=0.11	-0.3% (-0.8 to 0.2%) P=0.28	60 ml (-10 to 130 ml) P=0.12	-30 ml (-80 to 10 ml) P=0.15	0.1% (-0.2 to 0.4%) P=0.48

Predicted differences in lung volumes were adjusted for age, gender, height, weight, body mass index, race or ethnic group, level of education attained and current smoking status. Airway wall thickness and percent airway wall thickness were evaluated in separate models. Predicted mean differences for the linear term were estimated using generalized estimating equations. Percent airway wall thickness was calculated as the airway wall thickness divided by the total airway diameter multiplied by 100.

Abbreviations: CI denotes confidence interval, SD standard deviation, RV residual volume, TLC total lung capacity, FRC functional residual capacity, and IC inspiratory capacity.

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e-Table 4. Differences in Absolute Lung Volumes and Odds of Absolute Lung Volumes being Above or Below the Limit of Normal by Percent Emphysema$_{<-950HU}$ with additional adjustment for Airway Lumen Diameter.

	Predicted difference in lung volume* (95% CI)				
	RV (ml)	**RV/TLC (%)**	**FRC (ml)**	**TLC (ml)**	**IC/TLC (%)**
Per SD increment in percent emphysema$_{<-950HU}$	250 ml (170 to 340 ml) P<0.001	3.1% (1.7 to 4.5%) P<0.001	250 ml (180 to 330 ml) P<0.001	290 ml (210 to 370 ml) P<0.001	-1.4% (-0.5 to -2.2%) P=0.002
	Odds ratio for lung volumes above or below the limit of normal† (95% CI)				
	RV > ULN	**RV/TLC > ULN**	**FRC > ULN**	**TLC > ULN**	**IC/TLC < LLN**
Per SD increment in percent emphysema$_{<-950HU}$	2.4 (1.1 to 5.1) P=0.02	3.3 (1.8 to 6.0) P<0.001	2.7 (1.5 to 4.7) P<0.001	2.3 (1.3 to 3.9) P=0.002	1.8 (1.0 to 3.2) P=0.04

Predicted mean differences for the linear term and odds for the dichotomous term were estimated using generalized estimating equations. *Predicted mean differences in lung volumes were adjusted for age, gender, height, weight, body mass index, race or ethnic group, level of education attained, current smoking status, and airway lumen diameters. †ULN and LLN were calculated using age, gender, and height-based reference equations, hence logistic models were unadjusted.

Abbreviations: HU denotes Hounsfield units, CI confidence interval, SD standard deviation, RV residual volume, TLC total lung capacity, FRC functional residual capacity, IC inspiratory capacity, ULN upper limit of normal, and LLN lower limit of normal.

e-Table 5. Differences in Absolute Lung Volumes by Percent Predicted D_{LCO}/V_A.

Lung structure metric	Predicted difference in lung volume (95% CI)				
	RV (ml)	RV/TLC (%)	FRC (ml)	TLC (ml)	IC/TLC (%)
Per SD decrement in percent predicted D_{LCO}/V_A	310 ml (180 to 440 ml) P<0.001	3.2% (1.4 to 5.2%) P<0.001	310 ml (170 to 460 ml) P<0.001	370 ml (210 to 540 ml) P<0.001	-1.6% (-0.4 to -2.9%) P=0.01

Predicted differences in lung volumes were adjusted for age, gender, height, weight, body mass index, race or ethnic group, level of education attained and current smoking status. Predicted mean differences for the linear term were estimated using generalized estimating equations.

Abbreviations: D_{LCO}/V_A denotes diffusing capacity of carbon monoxide in lung divided by alveolar volume, CI confidence interval, SD standard deviation, RV residual volume, TLC total lung capacity, FRC functional residual capacity, and IC inspiratory capacity.