

Percent Emphysema and Daily Motor Activity Levels in the General Population

Multi-Ethnic Study of Atherosclerosis

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e-Appendix 1

METHODS

IRB committee names and project approval numbers

1. Wake Forest University Institutional Review Board: Human Protocol: BG00-035
2. Columbia University Medical Center Institutional Review Board IRB #2: Protocol #: AAAA7791
3. Johns Hopkins University Institutional Review Board: Study #: NA_00030361
4. University of Minnesota Institutional Review Board: IRB Study Number: 9805M00034
5. Northwestern University Office for the Protection of Research Subjects: IRB Project Number: STU00021057
6. UCLA Office of the Human Research Protection Program: UCLA IRB #99-11- 057-24
7. University of Washington Human Subjects Division Review Committee: Application No.: 14122

Imaging

The CT scan acquisition followed the SPIROMICS/MESA-Lung full-inspiration protocol (0.984 pitch, 0.5 seconds, 120 kVp; 180mA for BMI of 20-30 kg/m², 145 mA for lower BMI and 270mA for higher BMI, with a 0.625mm reconstruction).¹ Calibration of scanners was confirmed with monthly lung phantom measures throughout the study.

Actigraphy

Acceleration detection had a range of 0.5 to 2 G peak values with a sensitivity of 0.025 G (0.245m/s²) and used a solid-state piezoelectric accelerometer. Sampling rate was 32 Hz. Epoch length of recording was variable and was set to 30 seconds.

For any given active energy expenditure time spent on a certain activity can be calculated based on our participants mean body weight of 79.4kg and on published² metabolic equivalent of task (MET=1kcal*kg⁻¹*h⁻¹; for example a person of 79.4kg walking on level ground with a at 3 mph pace, which equals about 3.3 METs, for one hour has an active energy expenditure of 79.4kg*1h*3.3 MET=262kcal=1097kJ).

Self-reported Physical Activity

The MESA Typical Week Physical Activity Survey was based on the Cross-Cultural Activity Participation Study,³ and assesses the physical activities during a typical week in the past month. It has been successfully used to show significant associations between physical activity and cardiovascular events.⁴ To estimate the individual's active energy expenditure, the time spent in each activity was then multiplied by its estimated Metabolic Equivalent of Task (MET) level.²

Covariates

Current smokers were defined by self-reported cigarette consumption in the past 30 days or cotinine levels >100 ng/ml.⁵ The threshold for never smoking was set to a lifelong consumption of 100 cigarettes or less. Hypertension was defined as blood pressure greater than 140/90 mmHg, anti-hypertensive medication usage or self-reported hypertension. Diabetes was defined according to the American Diabetes Association criteria (fasting plasma glucose ≥ 126 mg/L (7 mmol/L)) or use of antidiabetic drugs. History of myocardial infarction and heart failure were self-reported and adjudicated by two physicians based on requested medical records and pre-specified criteria.⁶

Statistical Analysis

Multivariable linear regression included age, gender, race/ethnicity, education and scanner manufacturer, height, weight, BMI category (as used for mA adjustment of the CT scans), FEV₁ and cotinine level and pack-years and, in secondary analyses, left ventricular ejection fraction (LVEF), and coronary artery calcium as covariates. We also restricted analyses to those with emphysema, or to those without COPD or a history of myocardial infarction or heart failure and stratified analyses by smoking status, gender, age, race/ethnicity, BMI, site, cardiac measures, diabetes mellitus, total cholesterol and oxygen saturation. Tests of interactions were performed by use of a likelihood ratio test in the full multivariate model.

e-Appendix 2

RESULTS

Percent Emphysema and Mean Activity Count on Actigraphy

e-Table 1. Difference between Q2 and Q4 in the full model (Table 2) for time spent walking at 3.3 MET.

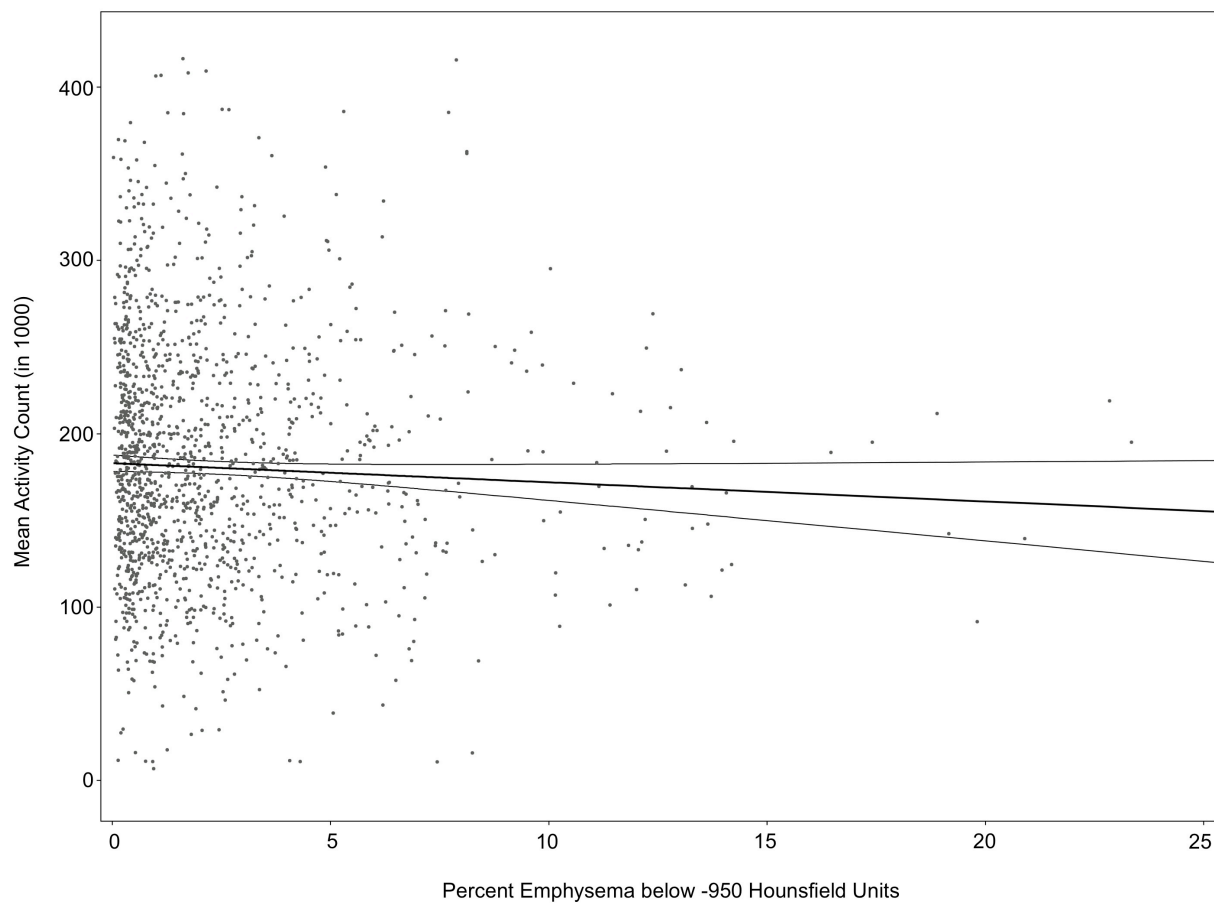
	Q1	Q2	Q3	Q4	Q5
Mean activity count/day	196321	189372	184321	179957	173799
Estimated Mean activity expressed in kcal/day = $(AC - 68579) / 166.07$	769	727	697	671	634
Conversion kcal to kJ	3218	3043	2916	2806	2651
Time equivalent in hours/day for walking at 3.3 MET (1097 kJ/79.4kg/h)*	2.93	2.77	2.66	2.56	2.42
Time equivalent in hours/week for walking at 3.3 MET (1097 kJ/79.4kg/h)*	20.54	19.42	18.61	17.91	16.92
Difference Q2-Q4 in hours per week			1.51		

*Assuming no other physical activity.

Sample calculation for difference between the mean activity counts (AC) in Q2 and Q4 in the full Model (Table 2) for time spent walking at 3.3 MET. Calculations are based on the following formulas: $y[\text{activity counts}] = 166.07 \times [\text{kcal}] + 68579$ and $1\text{kcal} = 4.184\text{kJ}$ (ISO31-4 standard) as well as active energy expenditure calculated for average participant with 79.4kg walking on level ground for one hour at a 3 mph pace = (3.3 METs) $\text{pace} = 79.4\text{kg} \times 1\text{h} \times 3.3\text{ MET} = 262\text{kcal} = 1097.00\text{ kJ}$.

For comparison the change per 1SD log%emphysema (=1.15) is 8099 AC and is equivalent to 1.3 hours of walking at a 3 mph pace per week.

e-Figure 1. Robust fit and scatter plot for mean activity count and percent emphysema



Robust fit plot and scatter plot for mean activity count and untransformed percent emphysema in the unadjusted model. $n=1435$. (coefficient (95% CI) in thousands: -1.1 ($-2.4, 0.2$) $p=0.088$. Results for the full model are: -1.7 ($-3.3, -0.1$); $p=0.04$)

e-Appendix 3

RESULTS

Percent Emphysema and Self-reported Activity Levels

e-Table 2 summarizes the characteristics of the 2716 participants with measures of percent emphysema and self-reported activity level, stratified by quintile of percent emphysema.

Although there was an inverse association of percent emphysema with self-reported moderate and vigorous activity levels, results did not attain statistical significance (e-Table 3). There was no association in the sample restricted to those with additionally available actigraphy measures (e-Table 4). Stratified results demonstrated a generally inverse association (e-Figure 2).

e-Table 2. Characteristics of study participants of MESA Exam 5 with self-reported activity level. Stratified by quintile of percent emphysema.

<i>Characteristic</i>	<i>Quintile of Percent Emphysema</i>				
	1	2	3	4	5
Quintile					
N participants	543	543	544	543	543
Percent emphysema	0.3	0.7	1.5	2.7	6.1
Participants with %emphysema > upper limit of normal -%	0	1	3	10	34
Self-reported activity level in MET*min/week (median (IQR))	2820 (1350, 5700)	3090 (1500, 5550)	2906 (1459, 5604)	2925 (1470, 5625)	3180 (1455, 5728)
Age – years	67±9	69±9	69±9	69±9	71±9
Male sex - %	22	34	49	61	77
Race or ethnic group – %					
Caucasian	25	31	37	43	55
African American	28	28	27	27	21
Hispanic	35	28	21	15	10

Chinese	12	13	15	15	14
Cigarette smoking –%					
Never smoker	54	54	45	42	34
Former smoker	35	37	47	49	56
Current smoker	11	9	8	9	10
Pack years of smoking in ever-smokers	12 (2, 31)	12 (2, 30)	16 (3, 35)	15 (3, 30)	20 (6, 39)
Height – cm	161±9	163±10	165±10	168±9	171±9
Weight – kg.	78±17	77±18	79±18	80±18	78±17
BMI – kg/m ²	29.9±5.6	28.9±5.7	28.6±5.6	28.2±5.2	26.7±4.6
Diabetes - %	24	20	19	14	13
COPD – % (n=2292)	3	4	7	10	28
Hypertension - %	61	63	60	61	51
Ejection fraction <55% - % (n=2037)	13	16	16	16	24
Coronary calcification (any) - % (n=2398)	61	66	70	71	73
Beta-blocker use- %	22	19	19	18	12
Pulmonary function; Pre-bronchodilator spirometry:					
FEV ₁ – % predicted	92±19	97±31	95±19	98±20	94±23
FVC – % predicted	91±17	97±35	97±17	100±18	102±18
FEV ₁ to FVC ratio	0.77±0.07	0.76±0.08	0.74±0.08	0.74±0.08	0.68±0.11

Values are given in median and interquartile range in (IQR) parentheses. Plus-minus values are means ± standard deviation. Race or ethnic group, smoking status, and pack-year history were self-reported.

Abbreviations: COPD denotes chronic obstructive pulmonary disease; defined by post-bronchodilator FEV₁/FVC ratio of <0.7, Disease, FEV₁ forced expired volume in the first second, FVC forced vital capacity, and HU Hounsfield units.

e-Table 3. Self-reported activity level and emphysema by quintile of percent emphysema and mean differences per 1 log-unit change in percent emphysema.

Quintile	Mean absolute self reported activity in MET*min/week according to quintile of percent emphysema					Mean difference self reported activity (95% CI) per 1 log-unit increase of percent emphysema	p-value
	1	2	3	4	5		
Unadjusted							
Model n=2716	3911	3943	3964	3983	4011	+30 (-78, +139)	0.58
Minimally adjusted model*							
Model n=2716	3929	3851	3797	3752	3682	-76 (-202, +51)	0.24
Fully adjusted model†							
Model n=2499	3834	3749	3689	3639	3562	-83 (-220, +53)	0.23
Cardiac adjusted model‡							
Model n=1612	3812	3671	3571	3488	3360	-139 (-303, +31)	0.11

Units: MET*min/week

* Model includes age, gender, race/ethnicity, education and scanner manufacturer as covariates.

† Model also adds height, weight, BMI category, FEV1, cotinine level and pack-years.

‡ Fully adjusted model plus left ventricular ejection fraction and coronary calcium (Agaston) score.

MET*min/week according to quintile of percent emphysema are adjusted as indicated by the model.

e-Table 4. Self-reported activity level and emphysema by quintile of percent emphysema and mean differences per 1 log-unit change in percent emphysema restricted to participants with actigraphy

Quintile	Mean absolute self reported activity in MET*min/week according to quintile of percent emphysema					Mean difference self reported activity (95% CI) per 1 log-unit increase of percent emphysema	p-value
	1	2	3	4	5		
Unadjusted							
Model n=1386	4038	4044	4049	4053	4059	+7 (-145, +163)	0.93
Minimally adjusted model* n=1386	4044	3992	3954	3921	3875	-52 (-235, +129)	0.56
Fully adjusted model† n=1273	3978	3934	3901	3874	3835	-45 (-241, +152)	0.66
Cardiac adjusted model‡ n=862	4106	3995	3915	3847	3751	-111 (-347, +125)	0.36

Units: MET*min/week

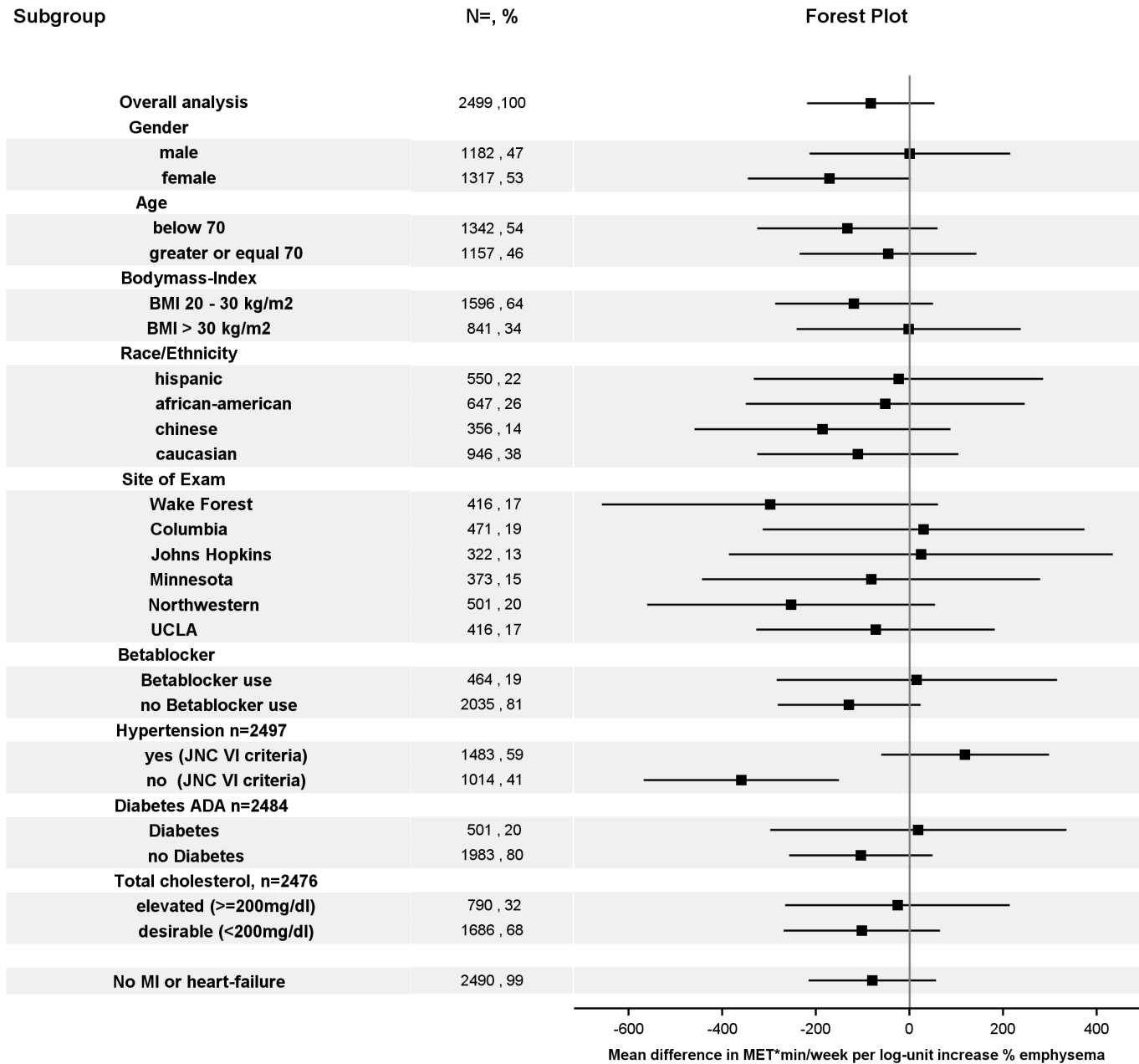
* Model includes age, gender, race/ethnicity, education and scanner manufacturer as covariates.

† Model also adds height, weight, BMI category, FEV1, cotinine level and pack-years.

‡ Fully adjusted model plus left ventricular ejection fraction and coronary calcium (Agaston) score.

MET*min/week according to quintile of percent emphysema are adjusted as indicated by the model.

e-Figure 2. Sensitivity Analysis for association of percent emphysema and self-reported activity level



Units: MET*min/week

Analysis for the fully adjusted model which includes age, gender, race/ethnicity, education, scanner manufacturer, height, weight, BMI category, cotinine, pack-years, and FEV1. Age, site and hypertension had a significant interaction (p < 0.05).

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