CHEST Online Supplement

Quantitative Emphysema on Low-Dose CT Imaging of the Chest and Risk of Lung Cancer and Airflow Obstruction

An Analysis of the National Lung Screening Trial

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e-Table 1. Multivariable Cox Regression Model of Lung Cancer Mortality

	Hazard Ratio (95% CI)	p-value
Age (per 1-yr increase)	1.08 (1.04-1.13)	<0.001
Body mass index[#]		
• Linear term	0.99 (0.94-1.04)	0.61
• Quadratic term	1.00 (1.00-1.00)	0.78
Smoking pack-years (per 1-unit increase)	1.01 (1.01-1.02)	<0.001
Time since smoking cessation (per 1-yr increase)	0.87 (0.82-0.93)	<0.001
Family history of lung cancer (yes vs. no)	1.57 (1.02-2.43)	0.042
%LAA (per 1% increase)*	1.02 (1.00-1.05)	0.045

[#] Body mass index is centered on the mean (28.0 kg/m^2) to avoid collinearity between linear and quadratic terms

* %LAA: % low attenuation area (defined as the percent of lung volume with voxels < -950 Hounsfield Units on computed tomography of the chest)

e-Table 2. Multivariable Cox Regression Model of All-Cause Mortality

	Hazard Ratio (95% CI)	p-value
Age (per 1-yr increase)	1.09 (1.07-1.11)	<0.001
Female (vs. male)	0.70 (0.57-0.87)	0.001
Race and ethnicity		
• Non-Hispanic White	1.00 [reference group]	
• Non-Hispanic Black	2.34 (1.67-3.29)	<0.001
• Hispanic or other	0.68 (0.37-1.25)	0.22
Body mass index#		
• Linear term	1.00 (0.98-1.02)	0.88
• Quadratic term	1.00 (1.00-1.00)	0.02
Smoking pack-years (per 1-unit increase)	1.01 (1.01-1.01)	<0.001
Time since smoking cessation (per 1-yr increase)	0.96 (0.94-0.98)	<0.001
Family history of lung cancer (yes vs. no)	1.17 (0.94-1.46)	0.16
%LAA (per 1% increase)*	1.01 (1.00-1.03)	0.042

Body mass index is centered on the mean (28.0 kg/m^2) to avoid collinearity between linear and quadratic terms

* %LAA: % low attenuation area (defined as the percent of lung volume with voxels < -950 Hounsfield Units on computed tomography of the chest)

e-Table 3. Airflow obstruction on spirometry by %LAA group (> 1% vs. ≤ 1%) in different age and sex subgroups

FEMALE < 65 YEARS			
	$FEV_1/FVC < 0.7$	$FEV_1/FVC \geq 0.7$	Total	Sensitivity 50.8% (95% CI 44.5%- 57.2%)
%LAA > 1%	120	124	244	Specificity 81.9% (95% CI 79.0%-84.8%)
% LAA ≤ 1%	116	561	677	PPV 49.2% (95% CI 42.9%-55.5%)
Total	236	685	921	NPV 82.9% (95% CI 80.0%-85.7%)

FEMALE ≥ 65 YEARS			
	$FEV_1/FVC < 0.7$	$FEV_1/FVC \geq 0.7$	Total	Sensitivity 65.3% (95% CI 56.8%-73.8%)
%LAA > 1%	79	57	136	Specificity 72.6% (95% CI 66.5%-78.7%)
% LAA ≤ 1%	42	151	193	PPV 58.1% (95% CI 49.8%-66.4%)
Total	121	208	329	NPV 78.2% (95% CI 72.4%-84.1%)

MALE < 65 YEARS			
	$FEV_1/FVC < 0.7$	$FEV_1/FVC \geq 0.7$	Total	Sensitivity 61.6% (95% CI 56.4%-66.7%)
%LAA > 1%	210	183	393	Specificity 72.5% (95% CI 69.1%-75.9%)
% LAA ≤ 1%	131	483	614	PPV 53.4% (95% CI 48.5%-58.4%)
Total	341	666	1007	NPV 78.7% (95% CI 75.4%-81.9%)

MALE ≥ 65 YEARS			
	$FEV_1/FVC < 0.7$	$FEV_1/FVC \geq 0.7$	Total	Sensitivity 74.2% (95% CI 56.4%-66.7%)
%LAA > 1%	144	85	229	Specificity 65.9% (95% CI 60.0%-71.8%)
% LAA ≤ 1%	50	164	214	PPV 62.9% (95% CI 56.6%-69.1%)
Total	194	249	443	NPV 76.6% (95% CI 71.0%-82.3%)

%LAA: % low attenuation area (defined as the percent of lung volume with voxels < -950 Hounsfield Units on computed tomography of the chest); FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; CI: confidence intervals; PPV: positive predictive value; NPV: negative predictive value.

e-Table 4. Associations between each of %LAA and FEV$_1$/FVC < 0.7 with lung cancer incidence, lung cancer mortality and all-cause mortality in multivariable Cox regression models
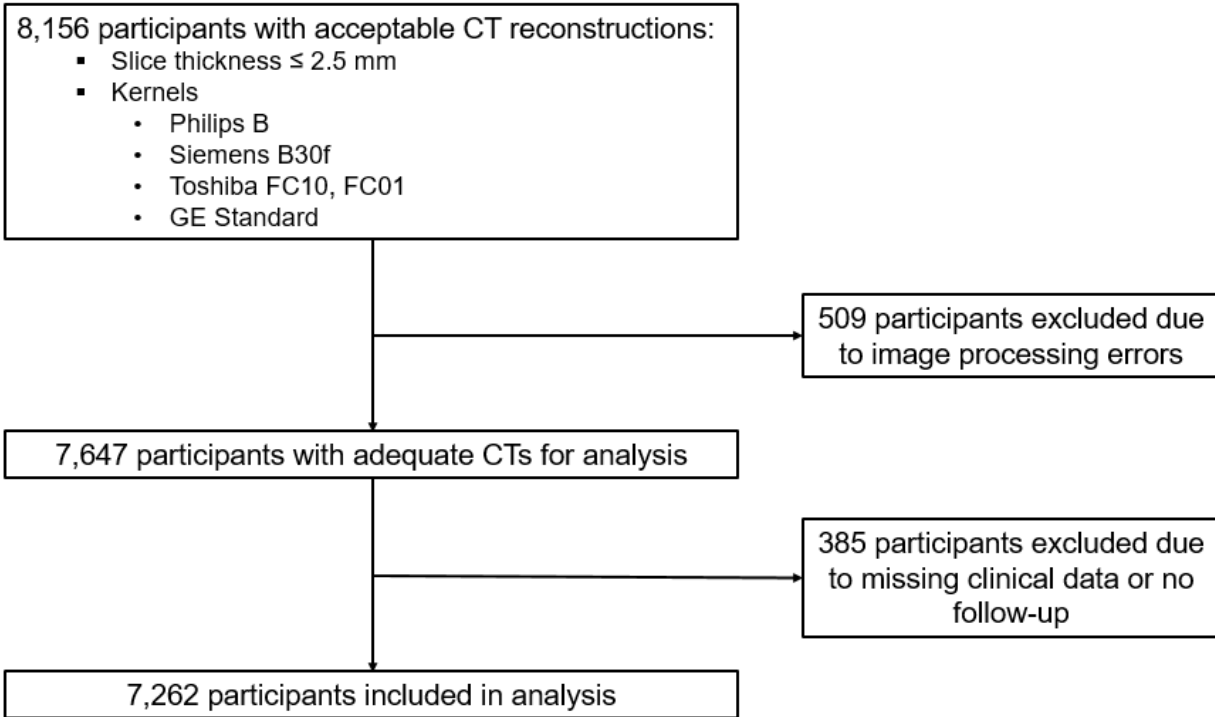
Outcome	%LAA*	FEV$_1$/FVC < 0.7^
Lung cancer incidence	HR 1.01 (1.00-1.03) p=0.14	HR 1.17 (0.85-1.60) p=0.33
Lung cancer mortality	HR 1.01 (0.98-1.04) p=0.64	HR 1.77 (1.03-3.05) p=0.04
All-cause mortality	HR 1.00 (0.98-1.02) p=0.83	HR 1.25 (0.91-1.72) p=0.16

%LAA: % low attenuation area (defined as the percent of lung volume with voxels < -950 Hounsfield Units on computed tomography of the chest); FEV$_1$: forced expiratory volume in the first second; FVC: forced vital capacity; HR: hazard ratio

*Cells represent hazard ratios with 95% confidence intervals and associated p-values for 1% increase in %LAA after adjustment for covariates.

^Cells represent hazard ratios with 95% confidence intervals and associated p-values for FEV$_1$/FVC < 0.7 (compared to FEV$_1$/FVC ≥ 0.7) after adjustment for covariates.

e-Figure 1. Consort Diagram

8,156 participants with acceptable CT reconstructions:
- Slice thickness ≤ 2.5 mm
- Kernels
  - Philips B
  - Siemens B30f
  - Toshiba FC10, FC01
  - GE Standard

509 participants excluded due to image processing errors

7,647 participants with adequate CTs for analysis

385 participants excluded due to missing clinical data or no follow-up

7,262 participants included in analysis

e-Figure 2. Histograms of %LAA in participants with and without airflow obstruction