

Diffusing Capacity of Carbon Monoxide in Assessment of COPD

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e-Table 1. Baseline characteristics and outcomes of participants missing % emphysema (%LAA₋₉₅₀)

Characteristic	Total (N=1806)	Analysis (N=1564)	Missing (N=242)
Age	68 (62, 74)	68 (62, 74)	68 (63, 74)
Male, N (%)	984 (54%)	841 (54%)	143 (59%)
Black, N (%)	356 (20%)	281 (18%)	75 (31%)
Education, N (%)			
High school, no diploma	143 (8%)	117 (7%)	26 (11%)
High school graduate or GED	442 (24%)	379 (24%)	63 (26%)
Some college or technical school, no degree	537 (30%)	467 (30%)	70 (29%)
College or technical school graduate (Bachelor's or Associate degree)	498 (28%)	437 (28%)	61 (25%)
Master's or doctoral degree	186 (10%)	164 (10%)	22 (9%)
BMI, kg/m ²	27 (24, 31)	28 (24, 31)	27 (23, 31)
Obese (BMI≥30), N (%)	589 (33%)	519 (33%)	70 (29%)
Anemia, N (%)	240 (13%)	197 (13%)	43 (18%)
Diabetes, N (%)	282 (16%)	249 (16%)	33 (14%)
Congestive Heart Failure, N (%)	76 (4%)	60 (4%)	16 (7%)
Sleep Apnea, N (%)	312 (17%)	280 (18%)	32 (13%)
Pack years of smoking	45 (34, 63)	45 (34, 63)	46 (35, 62)
Smoking Status, N (%)			
Former smoker	558 (31%)	484 (31%)	74 (31%)
Current to former smoker*	229 (13%)	191 (12%)	38 (16%)
Current smoker	1019 (56%)	889 (57%)	130 (54%)
FEV ₁ percent predicted	69 (50, 89)	70 (51, 89)	64 (42, 83)
DLCO percent predicted	65 (49, 81)	66 (50, 82)	57 (42, 74)
≤ 50%, N(%)	479 (27%)	388 (25%)	91 (38%)
KCO percent predicted	72 (57, 87)	73 (58, 87)	67 (51, 83)
≤ 50%, N(%)	304 (17%)	246 (16%)	58 (24%)
CAT	13 (7, 20)	13 (7, 20)	16 (8, 22)
SGRQ	29 (13, 46)	28 (13, 45)	35 (16, 53)
SF-36 Physical	42 (33, 50)	42 (33, 50)	39 (31, 49)
SF-36 Mental	55 (46, 60)	55 (46, 60)	55 (45, 60)
6MWD (feet)	1260 (982, 1500)	1280 (1000, 1512)	1180 (800, 1432)
%LAA ₋₉₅₀ [†]	4 (1, 14)	4 (1, 14)	-
LAA ₋₉₅₀ >5%, N (%) [†]	741 (47%)	741 (47%)	-
Airway Wall Thickness	1.1 (0.9, 1.2)	1.1 (0.9, 1.2)	1.1 (0.9, 1.3)
TLC (L)	5.8 (4.9, 6.9)	5.8 (4.9, 6.9)	5.2 (4.1, 6.3)
Resting oxygen saturation %	96 (94, 97)	96 (94, 97)	96 (94, 98)

Values are median (interquartile range) unless otherwise specified. *BMI*: body mass index; *FEV₁*: Forced expiratory volume in 1 second; *DLCO*: Diffusion capacity of the lung for carbon monoxide; *KCO*: gas transfer efficiency coefficient; *CAT*: COPD Assessment Test; *SGRQ*: St. George's Respiratory Questionnaire; *SF-36*: Short Form 36-item survey; *6MWD*: six-minute walk distance; %LAA₋₉₅₀: percent low attenuation areas ≤ -950 Hounsfield units consistent with emphysema; *TLC*: total lung capacity, estimated on CT scan

*Current to former smoker refers to the participants who went from being current smokers at the Phase I visit to former smokers by the Phase II visit.

† %LAA₋₉₅₀ characteristics are reported among the subset of participants with available HRCT data, N=1576.

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e-Table 2. Respiratory outcomes by DLCO and FEV₁ without adjustment for emphysema (%LAA-950)

Outcome	DLCO % predicted		FEV ₁ % predicted	
	Regression Coefficient (95% CI)	p-value	Regression Coefficient (95% CI)	p-value
CAT score	0.55 (0.4, 0.7)	<.001	1.14 (0.98, 1.3)	<.001
SGRQ score	2.01 (1.58, 2.43)	<.001	3.2 (2.84, 3.57)	<.001
Activity	3.17 (2.56, 3.79)	<.001	4.28 (3.82, 4.73)	<.001
Impact	1.55 (1.14, 1.96)	<.001	2.54 (2.12, 2.96)	<.001
Symptom	1.29 (0.71, 1.87)	<.001	3.39 (3.03, 3.75)	<.001
SF-36 Physical Function	-0.92 (-1.13, -0.71)	<.001	-1.32 (-1.59, -1.06)	<.001
SF-36 Mental	-0.06 (-0.36, 0.24)	0.676	-0.14 (-0.39, 0.12)	0.291
6MWD (feet)	-52.03 (-62.83, -41.24)	<.001	-42.72 (-48.25, -37.18)	<.001
Resting SpO ₂ %	-0.25 (-0.39, -0.12)	<.001	-0.18 (-0.23, 0.13)	<.001

Total population (n=1806) was utilized in this analysis. Associations are per 10% decrease in percent predicted DLCO or percent predicted FEV₁. Models include age, sex, BMI categories, ethnicity, education, smoking pack years, smoking status, anemia status, diabetes status, congestive heart failure status, sleep apnea status, % predicted FEV₁, and % predicted DLCO. 95% CI: 95% confidence interval; CAT: COPD Assessment Test; SGRQ: St. George's Respiratory Questionnaire; SF-36: Short Form 36-item survey; 6MWD: six-minute walk distance; SpO₂ %: oxygen saturation

e-Table 3. Respiratory outcomes by KCO and FEV₁ with adjustment for emphysema (%LAA-950)

Outcome	KCO % predicted		FEV ₁ % predicted	
	Regression Coefficient (95% CI)	p-value	Regression Coefficient (95% CI)	p-value
CAT score	0.59 (0.39, 0.79)	<.001	1.31 (1.1, 1.51)	<.001
SGRQ score	1.6 (1.15, 2.05)	<.001	3.39 (3.05, 3.74)	<.001
Activity	2.26 (1.46, 3.07)	<.001	4.68 (4.22, 5.14)	<.001
Impact	1.23 (0.8, 1.65)	<.001	2.6 (2.24, 2.95)	<.001
Symptom	1.68 (1.2, 2.16)	<.001	3.7 (3.35, 4.05)	<.001
SF-36 Physical Function	-0.72 (-1.05, -0.39)	<.001	-1.53 (-1.81, -1.24)	<.001
SF-36 Mental	-0.21 (-0.55, 0.13)	0.220	-0.02 (-0.33, 0.33)	0.920
6MWD (feet)	-35.66 (-47.6, -23.73)	<.001	-55.3 (-60.61, -49.99)	<.001
Resting SpO ₂ %	-0.18 (-0.36, 0)	0.045	-0.25 (-0.34, -0.16)	<.001

Total population (n=1564) was utilized in this analysis. Associations are per 10% decrease in percent predicted KCO or percent predicted FEV₁. Models include age, sex, BMI categories, ethnicity, education, smoking pack years, smoking status, anemia status, diabetes status, congestive heart failure status, sleep apnea status, % predicted FEV₁, and % predicted KCO. 95% CI: 95% confidence interval; CAT: COPD Assessment Test; SGRQ: St. George's Respiratory Questionnaire; SF-36: Short Form 36-item survey; 6MWD: six-minute walk distance; SpO₂ %: oxygen saturation

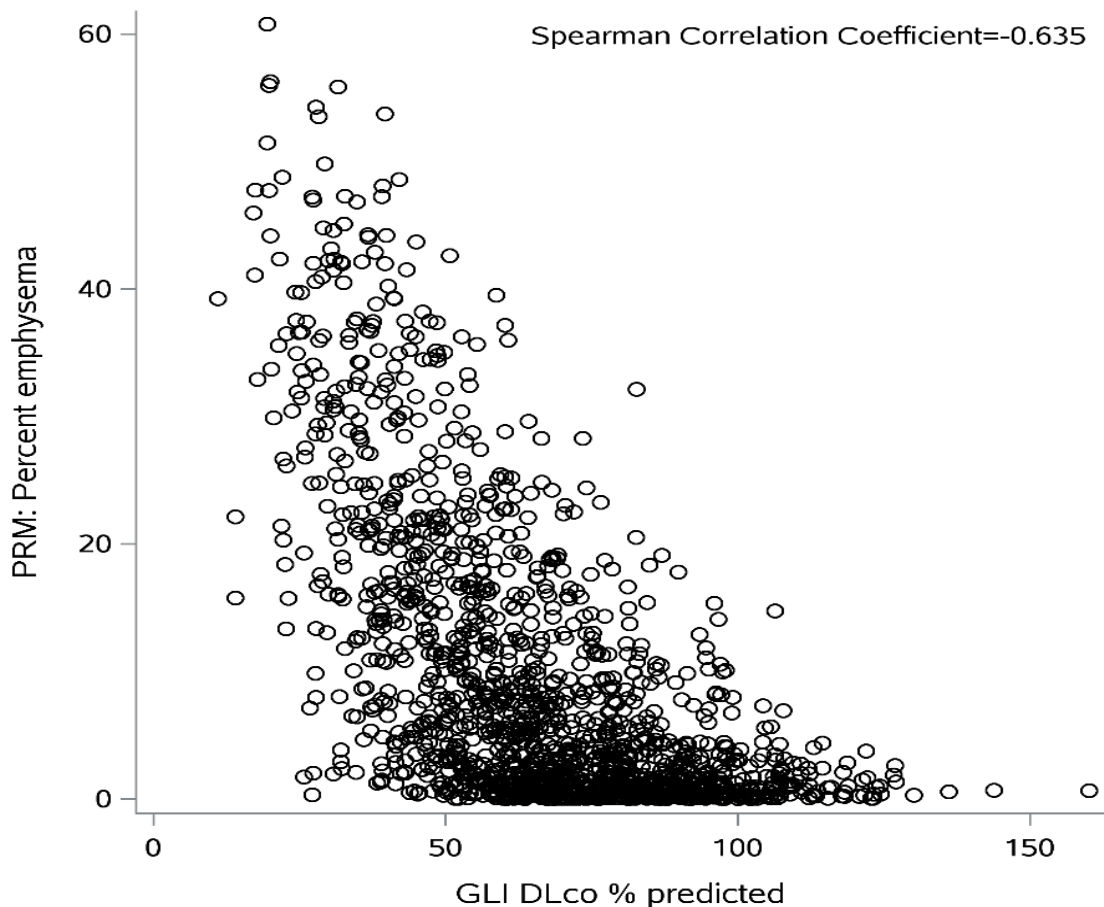
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e-Table 4. Percent Predicted KCO and FEV₁ associated with Exacerbations

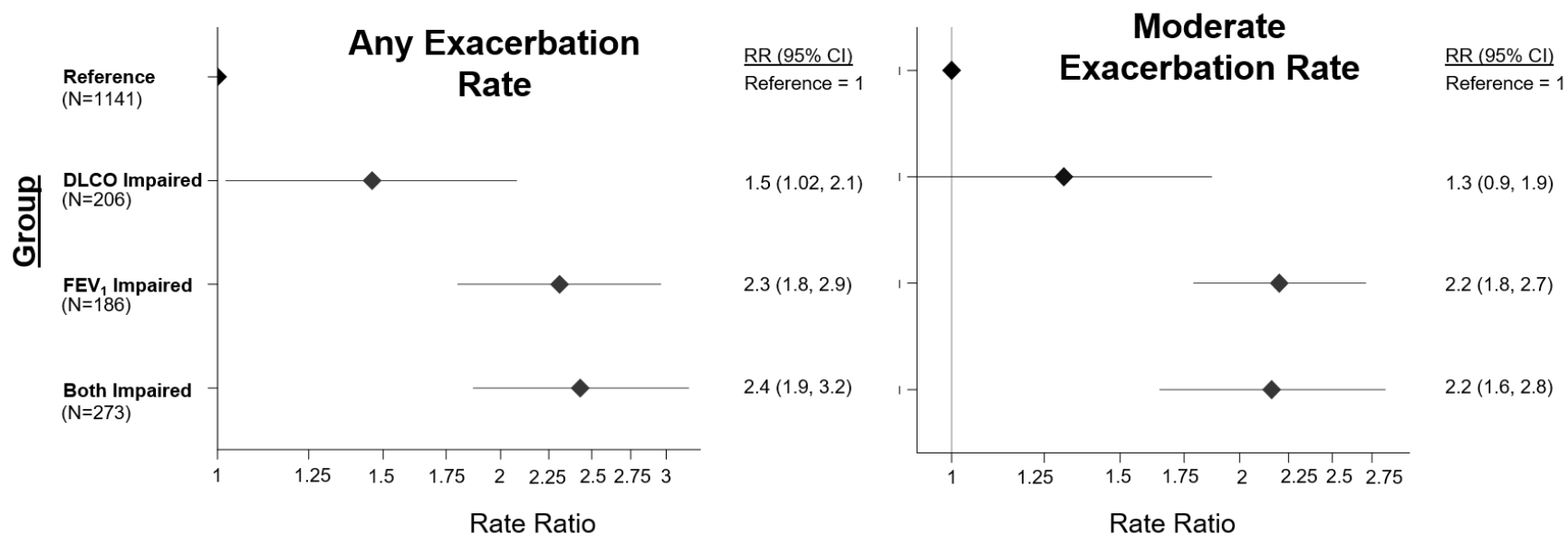
Outcome	KCO % predicted		FEV ₁ % predicted	
	Rate ratio (95% CI)	p-value	Rate ratio (95% CI)	p-value
Any exacerbations	1.06 (1, 1.12)	0.054	1.23 (1.19, 1.28)	<.001
Moderate exacerbations	1.04 (0.97, 1.14)	0.261	1.20 (1.16, 1.25)	<.001
Severe exacerbations	1.11 (1.05, 1.18)	<0.001	1.30 (1.22, 1.39)	<.001

Associations are per 10% decrease in percent predicted KCO or percent predicted FEV₁. Exacerbation models (N=1806) include age, sex, ethnicity, BMI categories, education, pack years, smoking status, diabetes status, anemia status, congestive heart failure status, sleep apnea status, emphysema as a categorical variable (missing data, ≤5% LAA-950, >5% LAA-950), % predicted KCO, and % predicted FEV₁. Any exacerbation refers to all episodes requiring antibiotics or steroids, moderate refers to only those episodes not resulting in an ER visit or hospitalization, and severe refers to those requiring an ER visit or hospitalization. 95% CI: 95% confidence interval

e-Figure 1. Scatterplot of DLCO and Percent Emphysema (%LAA-950)



e-Figure 2. Association between severe reduction in DLCO and FEV₁ with Exacerbations



Association between categories of FEV₁ and DLCO and self-reported rate of exacerbations. Any exacerbation refers to all exacerbations requiring antibiotics or steroids. Moderate exacerbation refers to any exacerbation requiring antibiotics or steroids but did not result in hospitalization. Groups are defined as reference (FEV₁ and DLCO both >50% predicted), DLCO impaired (FEV₁ >50% and DLCO ≤50%), FEV₁ impaired (FEV₁ ≤50% and DLCO >50%), and both impaired (FEV₁ and DLCO ≤50%). Model is adjusted for age, sex, ethnicity, BMI categories, smoking pack years, anemia status, diabetes status, congestive heart failure status, sleep apnea status, and emphysema as a categorical variable (missing, ≤5% LAA-950, >5% LAA-950). *RR*: Rate Ratio; *95% CI*: 95% confidence interval