Emphysema and extra-pulmonary tissue loss in COPD: A *Multi Organ Loss of Tissue* phenotype

Supplementary material.

The table S1 below shows findings in females and males for the variables reported in table 1 in the manuscript for the whole population. The results are similar independent of gender. Subjects in the most severe emphysema group LAA>25% represent the MOLT phenotype in both genders.

Females	Q1	Q2	Q3	Q4	
	LAA<7.5%	LAA 7.5–15%	LAA 15–25%	LAA≥25%	
	n=196	n=147	n=153	n=158	p-value
Demographics					
Age, years	*61 (7)*	*63 (7)*	*64 (7)*	*63 (6)*	*0.001*
BMI (kg/m^2)	*27 (7)*	*27 (7)*	*26 (6)*	*24 (4)*	*<0.001*
BMI (<21 kg/m^2) (%)	22%	15%	19%	27%	0.057
Fat-free Mass (kg)	*43 (8)*	*41 (8)*	*40 (8)*	*37 (7)*	*<0.001*
Fat-free Mass Index (kg/m^2)	*16.1 (2.6)*	*15.7 (2.6)*	*15.2 (2.6)*	*14.2 (2.4)*	*<0.001*
Smoking exposure					
Pack years	39 (22)	43 (20)	41 (22)	43 (21)	0.295
Current smoker (%)	*57%*	*37%*	*31%*	*20%*	*<0.001*
Symptoms					
mMRC dyspnea score	*1.4 (1.1)*	*1.7 (1.0)*	*1.9 (1.0)*	*1.9 (1.0)*	*<0.001*
SGRQ total score	*43 (21)*	*48 (17)*	*50 (16)*	*52 (15)*	*<0.001*
Previous exacerbations (patient/yr)	0.91	0.93	1.17	1.16	0.120
COPD Hospitalizations (patient/yr)	0.14	0.18	0.29	0.22	0.151
Self-reported comorbidities					
Cardiovascular disease	28%	27%	23%	22%	0.522
Chronic bronchitis	30%	30%	25%	21%	0.201
Osteoporosis	*19%*	*17%*	*27%*	*41%*	*<0.001*
Diabetes	*11%*	*8%*	*4%*	*1%*	*0.001*
Reflux/heartburn	29%	31%	33%	27%	0.654
Medications					
Inhaled corticosteroids	*64%*	*74%*	*77%*	*87%*	*<0.001*
Oral corticosteroids	<1%	1%	2%	<1%	0.546

Statins	19%	22%	11%	20%	0.070
Physiology					
Heart rate (bpm)	***77 (12)***	***80 (13)***	***81 (12)***	***78 (11)***	***0.011***
Systolic BP (mmHg)	130 (18)	134 (20)	134 (19)	130 (17)	0.072
Diastolic BP (mmHg)	***77 (10)***	***78 (12)***	***80 (13)***	***76 (10)***	***0.032***
FEV_1 (L)	***1.39 (0.38)***	***1.18 (0.34)***	***0.99 (0.32)***	***0.89 (0.30)***	***<0.001***
FEV_1 Percent predicted	***61 (13)***	***53 (13)***	***46 (14)***	***41 (13)***	***<0.001***
FVC (L)	2.49 (0.61)	2.50 (0.64)	2.38 (0.68)	2.36 (0.67)	0.121
FEV_1/FVC (%)	***56 (8)***	***47 (9)***	***42 (9)***	***38 (8)***	***<0.001***
Oxygen saturation (%)	***95.3 (2.7)***	***94.3 (3.4)***	***94.3 (2.8)***	***94.6 (2.8)***	***0.003***
6MWD (m)	***385 (113)***	***369 (103)***	***344 (125)***	***317 (128)***	***<0.001***
BODE index	***2.1 (1.8)***	***2.7 (1.9)***	***3.7 (2.2)***	***4.3 (2.1)***	***<0.001***
Circulating blood					
Hematocrit (%)	0.42 (0.04)	0.42 (0.03)	0.42 (0.04)	0.42 (0.03)	0.543
Hemoglobin (g/L)	139 (11)	140 (11)	140 (12)	141 (11)	0.603
WBC (10^9/L)	8.2 (2.6)	7.7 (2.3)	7.6 (2.6)	7.7 (2.3)	0.162
Neutrophils (10^9/L)	5.2 (2.2)	4.9 (2.1)	5.1 (2.4)	5.1 (2.1)	0.694
Eosinophils (10^9/L)	0.21 (0.20)	0.21 (0.14)	0.19 (0.14)	0.20 (0.14)	0.387
Fibrinogen (mg/dL)	437 [383–499]	444 [392–517]	474 [402–530]	449 [383–499]	0.164
CRP (mg/L)	2.7 [1.3–7.8]	3.0 [1.3–8.2]	3.3 [1.6–7.1]	2.4 [1.1–4.8]	0.088
IL-6 (pg/mL)	1.9 [0.5–4.1]	1.9 [0.2–4.6]	2.1 [0.6–4.0]	1.7 [0.7–3.4]	0.933
IL-8 (pg/mL)	***8.1 [4.2–15.1]***	***7.4 [3.1–13.8]***	***6.2 [3.2–10.4]***	***6.0 [3.1–11.8]***	***0.010***
CC-16 (ng/mL)	***4.1 [2.7–5.9]***	***4.0 [2.7–5.8]***	***4.3 [3.2–6.1]***	***4.8 [3.3–6.7]***	***0.013***
SP-D (ng/mL)	***122 [84–199]***	***117 [82–177]***	***112 [84–158]***	***110 [72–151]***	***0.009***
sRAGE (ng/mL)	***1.5 [1.1–1.9]***	***1.4 [1.0–1.8]***	***1.2 [0.9–1.5]***	***1.1 [0.8–1.4]***	***<0.001***
CCL-18 (ng/mL)	***95 [77–120]***	***100 [77–123]***	***111 [84–142]***	***99 [75–133]***	***0.037***

Males	Q1	Q2	Q3	Q4	
	LAA<7.5%	LAA 7.5–15%	LAA 15–25%	LAA≥25%	
	n=240	n=296	n=305	n=322	p-value
Demographics					
Age, years	*62 (8)*	*64 (7)*	*65 (6)*	*64 (7)*	*<0.001*
BMI (kg/m^2)	*28 (5)*	*28 (6)*	*27 (5)*	*25 (5)*	*<0.001*
BMI (<21 kg/m^2) (%)	*5%*	*9%*	*12%*	*23%*	*<0.001*
Fat-free Mass (kg)	*61 (10)*	*59 (10)*	*57 (10)*	*53 (11)*	*<0.001*
Fat-free Mass Index (kg/m^2)	*20.0 (2.8)*	*19.8 (3.1)*	*19.0 (3.1)*	*17.5 (3.0)*	*<0.001*
Smoking exposure					
Pack years	50(28)	51 (31)	55 (28)	51 (27)	0.213
Current smoker (%)	*54%*	*41%*	*30%*	*22%*	*<0.001*
Symptoms					
mMRC dyspnea score	*1.4 (1.0)*	*1.6 (1.1)*	*1.7 (1.0)*	*1.9 (1.0)*	*<0.001*
SGRQ total score	*43 (20)*	*46 (19)*	*48 (18)*	*54 (16)*	*<0.001*
Previous exacerbations (patient/yr)	*0.51*	*0.75*	*0.84*	*1.05*	*<0.001*
COPD Hospitalizations (patient/yr)	*0.14*	*0.22*	*0.17*	*0.29*	*0.013*
Self-reported comorbidities					
Cardiovascular disease	*35%*	*40%*	*39%*	*29%*	*0.018*
Chronic bronchitis	*38%*	*31%*	*34%*	*41%*	*0.037*
Osteoporosis	*1%*	*4%*	*7%*	*7%*	*0.002*
Diabetes	*13%*	*14%*	*13%*	*7%*	*0.024*
Reflux/heartburn	25%	24%	23%	20%	0.416
Medications					
Inhaled corticosteroids	*50%*	*67%*	*74%*	*85%*	*<0.001*
Oral corticosteroids	<1%	1%	<1%	2%	0.848
Statins	*26%*	*28%*	*28%*	*19%*	*0.029*
Physiology					
Heart rate (bpm)	*75 (14)*	*76 (13)*	*78 (14)*	*82 (13)*	*<0.001*
Systolic BP (mmHg)	135 (20)	134 (19)	134 (17)	132 (18)	0.352
Diastolic BP (mmHg)	80 (11)	79 (10)	80 (10)	80 (11)	0.928
FEV$_1$ (L)	*1.83 (0.51)*	*1.58 (0.48)*	*1.41 (0.50)*	*1.15 (0.42)*	*<0.001*
FEV$_1$ Percent predicted	*57 (14)*	*51 (14)*	*46 (15)*	*37 (13)*	*<0.001*
FVC (L)	3.42 (0.87)	3.37 (0.78)	3.41 (0.87)	3.34 (0.90)	0.646
FEV$_1$/FVC (%)	*54 (9)*	*47 (10)*	*41 (9)*	*34 (8)*	*<0.001*
Oxygen saturation (%)	*95.1 (2.5)*	*94.6 (3.3)*	*94.4 (3.3)*	*94.1 (2.9)*	*0.002*

6MWD (m)	*411 (113)*	*392 (124)*	*375 (115)*	*343 (117)*	*<0.001*
BODE index	*2.1 (1.7)*	*2.8 (1.8)*	*3.3 (2.0)*	*4.3 (2.1)*	*<0.001*
Circulating blood					
Hematocrit (%)	0.45 (0.04)	0.45 (0.04)	0.44 (0.04)	0.45 (0.04)	0.508
Hemoglobin (g/L)	149 (13)	149 (14)	148 (12)	150 (12)	0.484
WBC (10^9/L)	8.1 (2.5)	7.8 (2.2)	8.0 (2.4)	7.9 (2.1)	0.446
Neutrophils (10^9/L)	5.3 (2.1)	5.1 (1.8)	5.4 (2.2)	5.3 (1.7)	0.509
Eosinophils (10^9/L)	0.24 (0.20)	0.23 (0.16)	0.23 (0.16)	0.21 (0.16)	0.143
Fibrinogen (mg/dL)	430 [376–499]	438 [379–498]	449 [391–504]	454 [390–512]	0.074
CRP (mg/L)	3.3 [1.7–7.6]	3.7 [1.6–7.1]	3.6 [1.7–7.6]	3.2 [1.4–7.2]	0.852
IL-6 (pg/mL)	2.0 [0.4–4.8]	2.3 [0.6–5.1]	2.3 [0.6–5.2]	1.9 [0.2–4.6]	0.509
IL-8 (pg/mL)	7.7 [3.6–16.0]	7.3 [3.7–13.7]	7.2 [3.6–11.9]	6.9 [3.2–11.9]	0.208
CC-16 (ng/mL)	5.1 [3.5–7.2]	5.2 [3.7–7.5]	5.4 [3.9–7.2]	5.6 [4.0–7.2]	0.481
SP-D (ng/mL)	*137 [94–188]*	*122 [86–173]*	*123 [89–175]*	*116 [83–168]*	*0.044*
sRAGE (ng/mL)	*1.4 [1.0–1.9]*	*1.3 [1.0–1.7]*	*1.2 [0.9–1.7]*	*1.0 [0.8–1.3]*	*<0.001*
CCL-18 (ng/mL)	104 [84–132]	108 [83–141]	112 [90–140]	99 [75–133]	0.431