SUPPLEMENTAL MATERIALS

Pulmonary Fibrosis after COVID-19 is Associated with Severity of Illness and Blood Leukocyte Telomere Length

Supplemental Methods.

Study Design

We conducted a single-center prospective cohort study of adults age 21 years and older hospitalized between March 1, 2020 and May 15, 2020 with a positive SARS-CoV-2 RT-PCR nasopharyngeal swab and who required supplemental oxygen. The Columbia University Irving Medical Center (CUIMC) Institutional Review Board study protocol number is AAAR1916. Participants signed a written informed consent.

Recruitment and Enrollment

We identified prospective patients by chart review to exclude those with pre-existing ILD or a history of lung transplantation. We enrolled prospective participants by calling consecutive subjects meeting eligibility criteria based on their admission date, with sampling weighted to include approximately 50% survivors who underwent mechanical ventilation. We sought to enroll 70-100 participants based upon the capacity of the research team to recruit and assess participants during the 4-month follow-up study period of July and August 2020. Participants ambulated independently prior to hospitalization, did not live in a skilled-care facility prior to hospitalization, required supplemental oxygen therapy during their hospital stay, and were discharged to acute rehabilitation, subacute rehabilitation, or home. All participants were living at home prior to enrollment.

Electronic Medical Record Measurements

We obtained clinical data from the New York Presbyterian-CUIMC clinical data warehouse, which contains electronic data for inpatient and outpatient visits[1]. Patient data included demographics, diagnoses, procedures, medications, laboratory tests, vital signs and ventilator flowsheet data, and other clinical variables. Past medical history diagnoses were retrieved from the hospital admission notes and by using groups of ICD-10 diagnosis codes

according to the Clinical Classifications Software by the Healthcare Cost and Utilization Project[2]. We calculated the Sequential Organ Failure Assessment (SOFA) score during the first 24 hour of admission[3].

Chest Computed Tomography

Non-contrast high resolution chest CT scans (HRCT) were performed at maximal inspiration using either GE VCT 64 or GE Revolution CT750 HD instrument. Two chest radiologists (MS and BD) evaluated the scans for radiographic abnormalities associated with post-acute ARDS[4-6] and COVID-19[7-10], including ground glass opacities, intra-parenchymal opacities, non-emphysematous cysts, centrilobular nodules, reticulations, honeycombing, and traction bronchiectasis. Those with ≥5% involvement of reticulations or honeycombing, or the presence of traction bronchiectasis, were categorized as having fibrotic-like radiographic patterns. All others with ≥5% involvement of a lung quadrant were categorized as having non-fibrotic patterns. The radiographic abnormalities were scored using a semi-quantitative scoring system used by the ARDSnet investigators[4]. Radiographic abnormalities were assessed at 5 levels: the aortic arch, 1cm above the diaphragm, and three levels equally spaced between the aortic arch and diaphragm. Each level was divided into four lung quadrants, and scored within each quadrant as: 0=no involvement; 1= <5% involvement; 2= 5–25% involvement; 3=26–49% involvement; 4=50–75% involvement; and 5=greater than 75% involvement. The sum of the quadrant scores at each level was averaged across the five levels to determine the final score (range 0-20). For traction bronchiectasis, an airway abnormality that is difficult to quantify, each level was scored as either 0 or 1 for its absence or presence, respectively, for a maximum score of 5.

In addition to the radiologists' subjective scoring of fibrotic-like patterns, the University of Iowa imaging lab (Iowa City, IA, USA) used the adaptive multiple features method (AMFM) to

quantify HRCT scans for various lung features, including: ground glass opacity, ground glass-reticular, honeycombing, emphysema, or normal lung[11].

Clinical Measurements

Pulmonary function tests were performed on one of two pulmonary function machines (NDD EasyOne Pro, Andover MA; Vyaire Medical VMAX Encore, Mettawa IL). Pulmonary function testing and six-minute walk distance (6MWD) were assessed according to established guidelines[12,13]. Cough was assessed using a 100mm visual analogue scale[14]. Dyspnea was assessed using the UCSD shortness of breath questionnaire[15].

Frailty Measurements

We measured the five Fried Frailty domains: gait-speed, grip-strength, weight loss, low activity, and exhaustion. We measured grip-strength, gait-speed, and exhaustion, and using the traditional Cardiovascular Health Study (CHS) methodology[16]. Weight loss was calculated as the difference between their hospitalization admission weight and the measured weight during the follow up visit. We used the CHS cutoff of a decrease >10 lbs. to define the presence of weight loss. We assessed the physical activity domain on the basis of report of activities performed at four-moth follow-up using the Duke Activity Status Index (DASI)[17] instead of the the Minnesota Leisure Time Physical Activity Questionnaire[18], the original CHS measure of physical activity, as we have shown that the DASI improves the construct and predictive validity of frailty assessments in acute respiratory failure survivors[19]. We used previously validated DASI score cutoffs for low activity in older acute respiratory failure survivors (men ≤12.5; women ≤10)[19].

Each frailty domain is assigned 1 point if present and 0 points if absent based on the aforementioned cutoffs (range, 0-5). Consistent with CHS methodology, we defined the frailty phenotype as being frail in ≥3 of the five domains.

Genetic and Genomic Measurements

Since neither blood nor genomic DNA was available for all participants from the time of the acute illness, blood was collected from each participant at the 4 month follow-up visit. DNA was isolated from blood leukocytes using the Gentra Puregene Blood kit (Qiagen, Valencia CA). Leukocyte telomere length (LTL) was measured using a quantitative PCR assay and the RotoGene real-type PCR system (Qiagen)[20]. The LTL was expressed as a logarithm-transformed ratio of telomere to single-copy gene [ln(T/S)] and this value was compared to LTL from normal control subjects (n=201 unrelated multiethnic individuals from Dallas, TX, ranging in age from 19 to 89 years) to estimate an age-adjusted LTL percentile.

Missing Data

The Glasgow Coma Score, a component of the SOFA score, was missing for nearly all non-ICU patients, and we thus imputed a score of 15 for these participants based on previous literature[21]. Inflammatory markers ESR, CRP, LDH, Ferritin and D-dimer, had 6-12% missingness. We used the MICE function in R(v3.5.1) to perform multiple imputation using predictive mean matching for missing values[22]. There were six participants that could not perform the 6-minute walk test because they were non-ambulatory and one whose baseline heart rate was too high to safely perform the test. For the six participants who were non-ambulatory, we imputed 0 and ran a complete case analysis excluding the last participant. Three participants were unable to produce acceptable or reproducible DLCO measure. Therefore, we ran a complete case analyses using only participants with complete PFT data.

Statistical Analyses

We examined unadjusted associations of clinical and biomarker characteristics with no abnormalities, non-fibrotic pattern or fibrotic-like pattern using analysis of variance (ANOVA),

Kruskal Wallis, or chi-squared tests. We calculated correlation coefficients between continuous data using Spearman's method. We examined adjusted associations of fibrotic-like patterns with the hypothesized and biologically plausible independent variables that were associated with fibrotic-like patterns in unadjusted analyses. We used generalized covariate balanced propensity scores (CBPS) to adjust for potential confounders as has been done in prior studies[23], to avoid model overparameterization. We generated propensity scores predicting each of the independent variables of interest (**Table S6**) using the CBPS function in R(v3.5.1)[24]. To do so, we calculated CBPS for each independent variable by regressing it on a set of potential confounders. For all the independent variables, we included a list of common confounders, including age, sex, race/ethnicity, days since infection, body mass index, pack-years of smoking, and treatment with steroids while hospitalized in the generation of the CBPS. In addition, each CBPS score was generated with the other three independent variables of interest. For example, the SOFA CBPS included the common confounders (age, sex, etc.) plus LDH, days of mechanical ventilation, and telomere length. Thus, each GAM has only two variables: (1) the independent variable of interest and (2) the CBPS score for that variable, with collectively controls for the aforementioned potential confounders.

In the GAMs, we did not assume linear associations between continuous independent variables and risk of fibrotic-like abnormalities on CT scan, and instead estimated associations by a nonparametric locally weighted smoothing spline (LOESS). For lab values like LDH, we removed outliers beyond 2 standard deviations for the analysis. For independent variables without statistically significant non-linear associations with fibrotic-like abnormalities in the GAMs, we estimated adjusted odds ratios using logistic regression models. Conventional residuals and quantile residuals[25] showed no substantive bias, had a mean of zero, and demonstrated constant variance across the predicated values, predictors and propensity scores.

Since LTL may increase severity of illness[26], and since LTL may be affected by critical illness[27], we conducted sensitivity analyses: one estimating associations of LTL, admission

SOFA score, LDH, and duration of mechanical ventilation with fibrotic-like patterns without adjusting for the other three independent variables. The second sensitivity analysis was performed with a more conservative definition of fibrosis that comprised only traction bronchiectasis and honeycombing[28]. Covariates were found to be balanced in all propensity scores (see **Table S7**)[29,30]. Plots Analysis were performed using Stata/IC v16 (StataCorp) and R, v3.5.1.

Table S1. Demographic and clinical features of COVID-19 survivors.

	Total	Normal CT chest	Non-Fibrotic pattern	Fibrotic-like pattern	p-value*
Number	76	31 (41%)	13 (17%)	32 (42%)	
DEMOGRAPHICS					
Age, mean (SD)	54.0 (13.7)	51.8 (13.7)	60.6 (10.8)	53.4 (14.2)	0.14
Male (%)	45 (61%)	16 (52%)	4 (31%)	25 (78%)	**0.007**
Hispanic ethnicity	43 (57%)	14 (45%)	10 (77%)	19 (59%)	0.14
Race					0.17
White	30 (39%)	13 (42%)	4 (31%)	13 (41%)	
Black	22 (30%)	13 (42%)	4 (31%)	5 (16%)	
Asian	1 (1%)	0	0	1 (4%)	
Other	23 (30%)	5 (16%)	5 (38%)	13 (41%)	
Body Mass Index (kg/m^2), mean (SD)	32.2 (6.9)	34.2 (7.8)	32.7 (4.6)	30.1 (6.4)	0.07
GENOMIC FACTORS					
Leukocyte telomere length, percentile (IQR)	52 (49-68)	52 (50-81)	52 (52-82)	49.5 (40-52)	**0.01**
LTL <10th percentile, N	3 (4%)	0	0	3 (9%)	0.11
COMORBIDITIES					
Hypertension	41 (54%)	20 (65%)	5 (38%)	16 (50%)	0.24
Diabetes	25 (33%)	12 (41%)	6 (46%)	7 (22%)	0.20
COPD	4 (5%)	1 (3%)	0	3 (9%)	0.36
Asthma	18 (27%)	8 (26%)	4 (31%)	6 (19%)	0.65
Heart Disease	2 (3%)	1 (3%)	1 (8%)	0	0.17
Chronic Kidney Disease	7 (9%)	5 (16%)	0	2 (6%)	0.29
Smoking Status					
Ever	31 (41%)	16 (52%)	4 (31%)	11 (34%)	0.27
Active	2 (3%)	1 (3%)	0	1 (2%)	0.81
Pack Years (IQR)	15 (5-20)	15 (5-20)	4.25 (1 - 13.75)	20 (8-22.5)	0.34
CLINICAL FACTORS					
Admission SOFA Score, mean (SD)	4.1 (2.4)	2.9 (1.7)	4.5 (3.4)	5.3 (2.4)	**0.001**
Received Steroids	39 (51%)	10 (32%)	5 (38%)	24 (75%)	**0.002**
Received Anti IL-6R blocker**	17 (22%)	3 (10%)	1 (8%)	13 (41%)	**0.005**
Venous thromboembolism (by imaging)	12 (16%)	4 (13%)	1 (8%)	7 (22%)	0.42
Received Therapeutic Anticoagulation	25 (33%)	6 (19%)	3 (23%)	16 (50%)	**0.03**
Maximum Oxygen Requirement					**<0.001**
Nasal Cannula	23 (30%)	18 (58%)	4 (31%)	1 (3%)	
Non-Rebreather	17 (22%)	6 (19%)	5 (38%)	6 (19%)	
NIPPV or HFNC	4 (5%)	2 (7%)	0	2 (6%)	
Mechanical Ventilation	31 (41%)	5 (16%)	4 (31%)	22 (69%)	
MV plus ECMO	1 (1%)	0	0	1 (3%)	
Ventilator Days (IQR)	30.5 (12-42)	7 (6-9)	32.5 (20-41)	34 (14-42)	**<0.001**
Hospital days (IQR)	18 (7-35)	4 (4-12)	16 (9-26)	35 (24-54)	**<0.001**
Discharge Disposition					**0.001**
Home	54 (71%)	29 (94%)	10 (77%)	15 (47%)	
Acute Rehabilitation	19 (25%)	1 (3%)	2 (15%)	16 (50%)	
Subacute Rehabilitation	3 (4%)	1 (3%)	1 (8%)	1 (3%)	
Home-dwelling at 4 months	76 (100%)	31 (100%)	13 (100%)	32(100%)	1.00
OUTCOMES					
Oxygen use at 4 months	4 (5%)	1 (3%)	2 (15%)	1 (3%)	0.25
FVC, % predicted, mean (SD)	83.6 (19.7)	87.6 (21.9)	83.2 (13.6)	79.8 (19.2)	0.19
DL(CO), % predicted, mean (SD)	74.9 (42.1)	90.5 (24.5)	74.2 (16.7)	60.5 (16.6)	**<0.001**
6MWD, m, mean (SD)	364 (98)	355 (105)	370 (72)	370 (103)	0.82
6MWD, % predicted, mean (SD)	68 (18)	67 (19)	80 (18)	65 (16)	0.06
Change in weight,kg, † median (IQR)	-0.2 (-5.1 - 2.3)	1.2 (-0.9 - 5.2)	-2.1 (-4.6 - 1.7)	-3.5 (-11.6 - 0.3)	**<0.001**

Data are n (%) unless otherwise specified.

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; LDH, lactate dehydrogenase; IL-6R, interleukin 6 receptor; NIPPV, non-invasive positive pressure ventilation; HFNC, high-flow nasal cannula,

MV, mechanical ventilation; ECMO, extracorporeal membrane oxygenation; FVC, forced vital capacity; DL(CO), diffusion capacity for carbon monoxide; 6MWD, 6 minute walk distance
* Associated examined using Chi-square, ANOVA or Kruskall-Wallis where appropriate
**Either tocilizumab or sarulimab
† Change in weight calculated as weight (kg) measured at 4 month visit minus weight documented at hospital admission.

Table S2. Prevalence of HRCT Abnormalities.

	Total (n=76)	Non-Fibrotic Patterns (n=13)	Fibrotic-Like Patterns (n=32)
Any Abnormality	45 (59%)		
Non-Fibrotic Abnormalities*:			
Intraparenchymal opacities	1 (1%)	0	1 (3%)
Ground glass opacities	33 (43%)	13 (100%)	20 (62%)
Nonemphysematous cysts	1 (1%)	0	1 (3%)
Diffuse centrilobular nodules	0	0	0
Fibrotic Abnormalities*:			
Reticulations	30 (39%)	0	30 (94%)
Honeycombing	1 (1%)	0	1 (3%)
Traction Bronchiectasis	21 (28%)	0	21 (66%)

HRCT: high resolution computed tomography

* patterns are not mutually exclusive and participants with fibrotic-like patterns can also have non-fibrotic patterns.

Table S3. Demographics and Clinical Factors Between those with and without Fibrotic-Like Patterns on CT Scan

	Total	Normal or Non-Fibrotic Pattern	Fibrotic-Like Pattern	p-value*
Number	76	44 (58%)	32 (42%)	
DEMOGRAPHICS				
Age, mean (SD)	54.0 (13.7)	54.4 (13.4)	53.4 (14.2)	0.74
Male	45 (61%)	20 (45%)	25 (78%)	**0.004**
Hispanic ethnicity	43 (57%)	24 (55%)	19 (59%)	0.67
Race				0.08
White	30 (39%)	17 (39%)	13 (41%)	
Black	22 (30%)	17 (39%)	5 (16%)	
Asian	1 (1%)	0	1 (4%)	
Other	23 (30%)	10 (23%)	13 (41%)	
Body Mass Index (kg/m2), mean (SD)	32.2 (6.9)	34.2 (7.0)	30.1 (6.4)	**0.001**
Smoking Status				0.32
Ever	31 (41%)	20 (45%)	11 (34%)	
Active	2 (3%)	1 (2%)	1 (2%)	
Pack Years (IQR)	15 (5-20)	15 (5-20)	20 (8-22.5)	
GENOMIC FACTORS				
Leukocyte telomere length, percentile (IQR)	52 (49-68)	50 (50-79)	49.5 (40-52)	**0.002**
LTL <10th percentile, N	3 (4%)	0	3 (9%)	**0.04**
CLINICAL FACTORS				
Admission SOFA Score, mean (SD)	4.1 (2.4)	3.2 (2.0)	5.3 (2.4)	**<0.001**
Lactate Dehydrogenase U/L, mean (SD)	597 (295)	508 (252)	713 (308)	**0.003**
Received Steroids	39 (51%)	15 (34%)	24 (75%)	**0.001**
Received Anti IL-6R blocker**	17 (22%)	4 (9%)	13 (41%)	**0.001**
Venous thromboembolism (by imaging)	12 (16%)	5 (11%)	7 (22%)	0.21
Received Therapeutic Anticoagulation	25 (33%)	9 (20%)	16 (50%)	**0.007**
Required Mechanical Ventilation	32 (42%)	9 (20%)	23 (72%)	**<0.001**
Ventilator Days, median (IQR)	30.5 (12-42)	0 (0-0)	34 (14-42)	**<0.001**
Hospital days, median (IQR)	18 (7-35)	14 (7-39)	35 (14-42)	**<0.001**

Data are n (%) unless otherwise specified.
Abbreviations: IL-6R, interleukin 6 receptor;
* Associated examined using Chi-square, Students t-test or Wilcoxon rank-sum where appropriate
** Either tocilizumab or sarulimab
Change in weight calculated as weight (kg) measured at 4 month visit minus weight documented at hospital admission.

Table S4. Clinical features of COVID-19 survivors who underwent mechanical ventilation.

	Total	None	Non-Fibrotic Pattern	Fibrotic-Like Pattern	p-value
	N = 32	N = 5	N = 4	N = 23	
Ventilator support, Days	30.5 (12-42)	7 (6-9)	32.5 (20-41)	34 (14-42)	**<0.001**
PaO_2:FiO_2*, mean (SD)	166 (78)	166 (57)	165 (127)	166 (76)	0.99
Sequential Organ Failure Assessment (SOFA)	5.7 (2.3)	3.4 (0.55)	7.0 (0.82)	5.9 (2.4)	**0.03**
Positive End-Expiratory Pressure (cmH2O)*	15 (12-16)	12 (12-14)	14 (10-18)	15 (14-16)	0.33
Tidal Volume (per cc/kg ideal body weight)*	6.4 (5.9-7.3)	6.2 (6.1-7.0)	7.6 (5.6-8.1)	6.4 (5.7-6.8)	0.22
Received Steroids (%)	20 (62%)	2 (40%)	1 (25%)	17 (74%)	0.09
Prone Positioning (%)	9 (28%)	0	0	9 (39%)	0.09
Paralysis (%)	14 (44%)	0	1 (25%)	13 (57%)	**0.05**

Abbreviations: PaO2, partial pressure of arterial oxygen; FiO2, Fraction of inspired oxygen
*These represent the first measured data following intubation

Table S5. Prevalence of CT abnormalities, lung function, physical impairment, and respiratory symptoms.

Abnormality	N (%)
Any Imaging Pattern	45 (59%)
Fibrotic-Like Pattern	32 (42%)
Reduced FVC*	27 (36%)
Reduced FEV1/FVC*	4 (5%)
Reduced DLCO*	40 (53%)
Short 6MWD**	59 (78%)
Weight Loss >10% baseline	14 (18%)
Weight Loss >10 lbs†	21 (28%)
Slow Gait Speed†	18 (24%)
Weak Grip†	40 (53%)
Decreased Activity†	15 (20%)
Exhaustion†	15 (20%)
UCSD SOBQ ≥ 10	52 (68%)
Cough Score ≥ 20‡	11 (14%)

Abbreviations: FVC, forced vital capacity; FEV1, forced expiratory volume in one second; DLCO, diffusion capac.y for carbon monoxide; 6MWD, six-minute walk distance; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.
*A reduced FVC or FEV1/FVC was defined as being below the lower limit of normal (LLN) for each subject.
** A short 6MWD was defined as being <80 percent of their predicted values.
† Fried frailty domain criteria (see Supplemental methods).
‡Cough visual analog score

Table S6. Associations between independent variables of interest and fibrotic-like patterns in multivariable logistic regression

Variable	OR	95% CI	p-value
Male Sex	1.28	0.28 - 5.95	0.75
BMI, m^2/kg	0.91	0.80 - 1.04	0.13
Age-Adjusted Telomere length*	1.35	1.06 - 1.72	**0.01**
SOFA Score**	1.49	1.17 - 1.89	**0.002**
Lactate Dehydrogenase, U/L	1.24	1.08 - 1.43	**0.003**
Days on Mechanical Ventilation	1.07	1.03 - 1.12	**<0.001**

BMI: body mass index; SOFA: sequential organ failure assessment
All analyses are adjusted for propensity scores that comprised age, sex, race, BMI, admission SOFA score, admission LDH, telomere length, ventilator days and days between positive COVID PCR and CT scan,
* per 10% decrease in telomere length
** per 50-point increase in variable

Table S7. Spearman correlation between SOFA score, ventilator days, and age-adjusted percent telomere length and covariables before and after covariate-balancing propensity score.

SOFA score, hospital admission	**Pre-CBPS weighting**	**Post-CBPS weighting**
Age	0.027	0.140
Sex	0.316	0.080
Time from COVID+ nasal swab to CT scan, in days	0.220	0.166
Black/African American	-0.187	-0.027
Hispanic	0.249	0.037
Other	-0.010	-0.017
BMI	-0.178	-0.004
Smoking, pack-years	0.046	0.067
Steroid therapy	0.363	0.190
Telomere length	-0.333	-0.122
Ventilator days	0.531	0.166
Ventilator Days	**Pre-CBPS weighting**	**Post-CBPS weighting**
Age	-0.189	-0.166
Sex	0.326	0.159
Time from COVID+ nasal swab to CT scan, in days	0.293	0.128
Black/African American	-0.218	-0.064
Hispanic	0.235	0.128
Other	0.068	-0.044
BMI	-0.173	-0.046
Smoking, pack-years	-0.117	-0.040
Steroid therapy	0.125	0.175
Telomere length	-0.117	-0.101
SOFA score, day of admission	0.532	0.273
Telomere Length (TL)	**Pre-CBPS weighting**	**Post-CBPS weighting**
Age	-0.074	-0.015
Sex	-0.046	-0.045
Time from COVID+ nasal swab to CT scan, in days	-0.12	-0.075
Black/African American	-0.179	0.053
Hispanic	-0.173	-0.039
Other	0.088	-0.001
BMI	0.106	0.061
Smoking, pack-years	-0.117	-0.006
Steroid therapy	-0.142	-0.035
SOFA, day of admission	-0.333	-0.108
Ventilator days	-0.117	-0.054

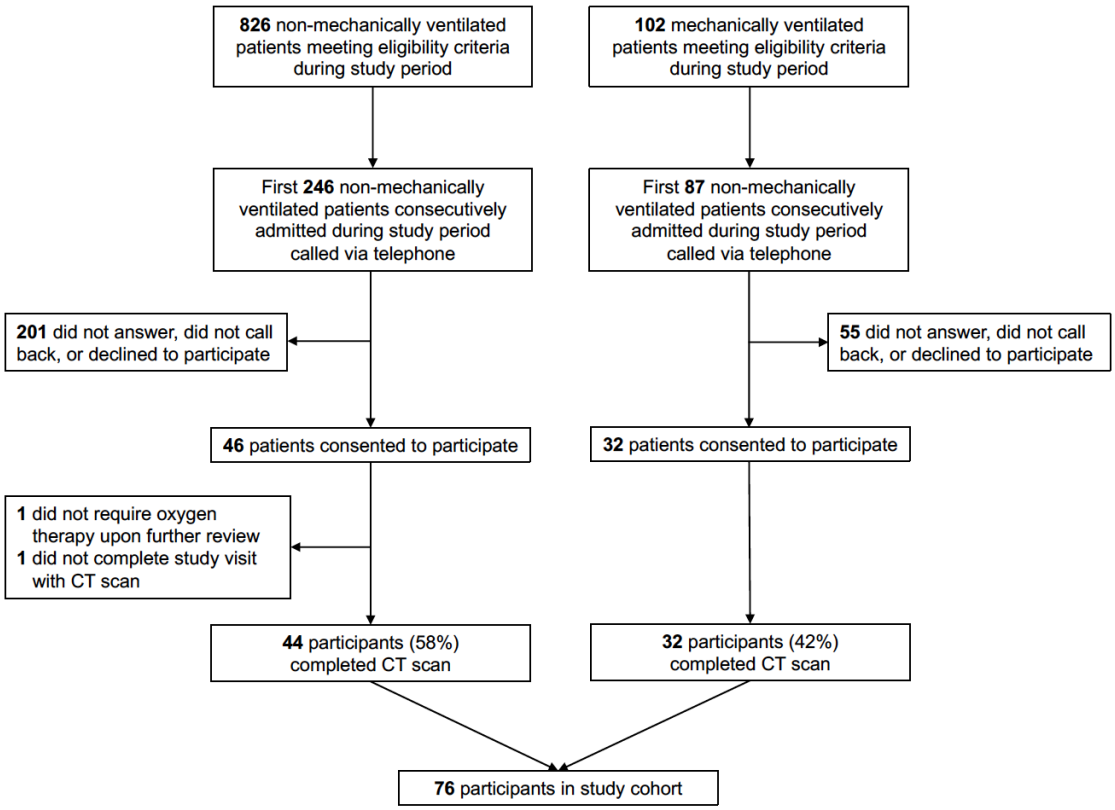

Figure S1. Study flow diagram

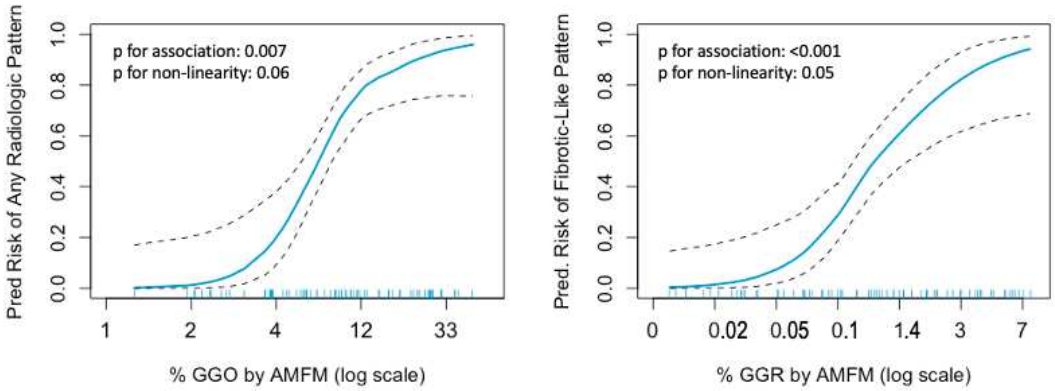

Figure S2. Continuous association of the natural log of the percent of Ground Glass Opacity (GGO) pattern as measured by Adaptive Multiple Features Method (AMFM) and the presence of any radiographic abnormality (left) and percent of Ground Glass Reticulation (GGR) pattern via AMFM and fibrotic-like pattern (right) using generalized additive models with LOESS smoothers. Both models are adjusted for age, sex, race/ethnicity and BMI.

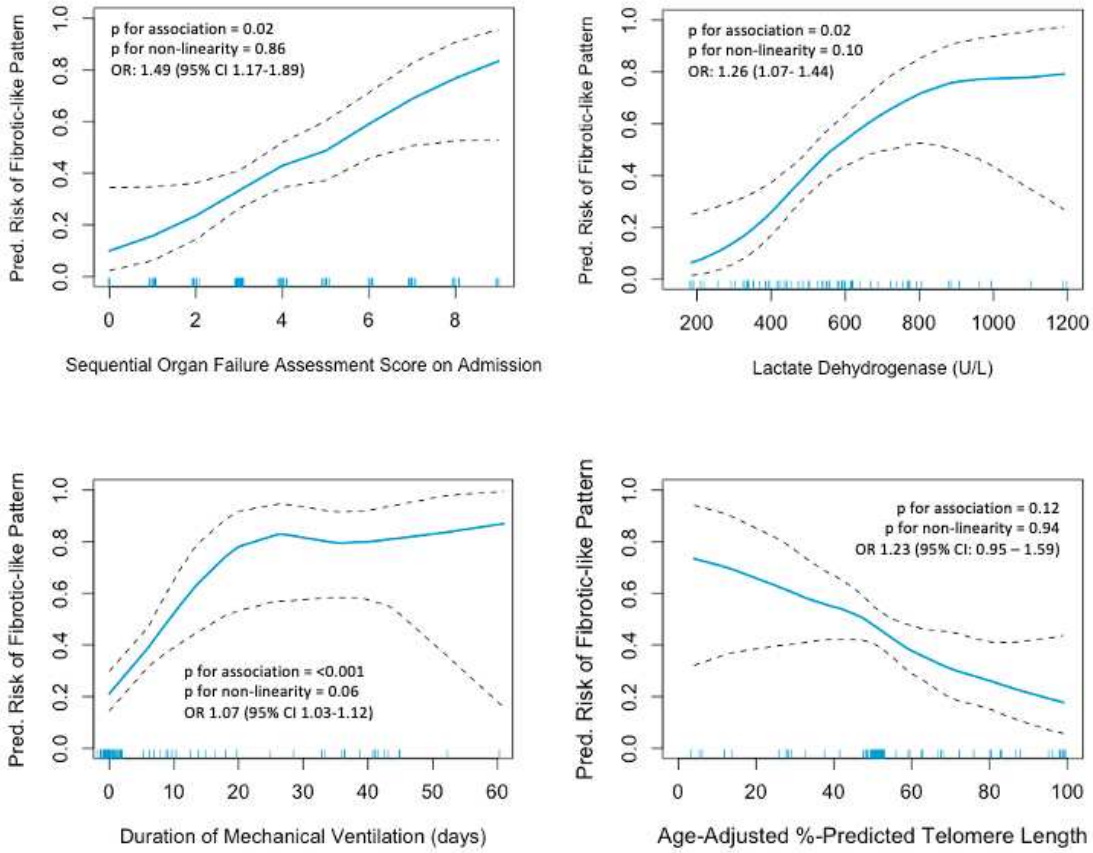

Figure S3. Sensitivity of the continuous association of fibrotic-like patterns on CT with SOFA score (top left), lactate dehydrogenase (top right), ventilator days (bottom left) and age-adjusted leukocyte telomere length percentile (bottom right) using generalized additive models with LOESS smoothers. Each model is adjusted for a common set of potential confounders (age, sex, race/ethnicity, days since infection, body mass index, pack-years of smoking and treatment with steroids while hospitalized), but not the other independent variables (SOFA score, LDH, days of mechanical ventilation, telomere length).

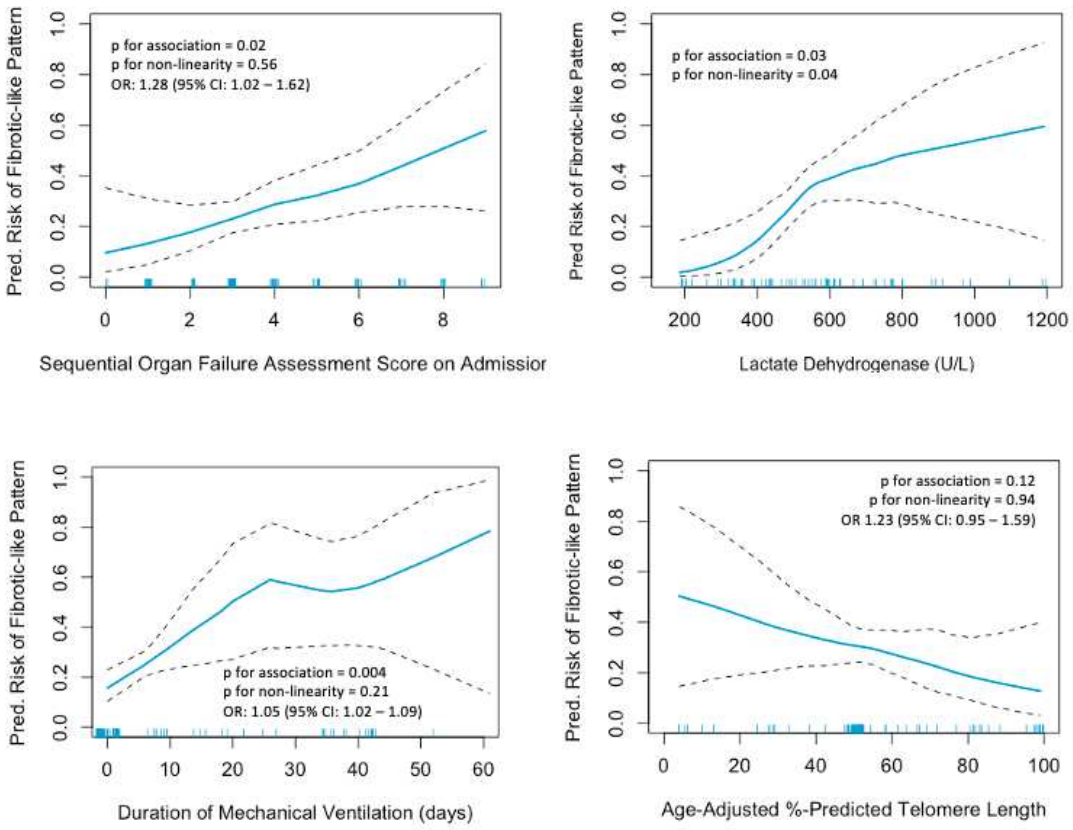

Figure S4. Sensitivity of the continuous association of fibrotic patterns on CT as defined by the presence of traction bronchiectasis or honeycombing with SOFA score (top left), lactate dehydrogenase (top right), ventilator days (bottom left) and age-adjusted leukocyte telomere length percentile (bottom right) using generalized additive models with LOESS smoothers. Each model is adjusted for a common set of potential confounders (age, sex, race/ethnicity, days since infection, body mass index, pack-years of smoking and treatment with steroids while hospitalized) and the other independent variables (SOFA score, LDH, days of mechanical ventilation, telomere length). The magnitude and shape of the associations do not appear meaningfully different from the main analysis where fibrotic-like radiographic abnormalities are defined as the presence of reticulations, traction bronchiectasis, or honeycombing.

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