Supplementary Material

Decreased peak expiratory flow rate associated with mortality in idiopathic pulmonary fibrosis: A preliminary report

Authors: Kohei Fujita M.D.[1], Hirotsugu Ohkubo M.D., Ph.D.[1], Akiko Nakano M.D., Ph.D.[2], Norihisa Takeda M.D., Ph.D.[1], Kensuke Fukumitsu M.D., Ph.D.[1], Satoshi Fukuda M.D., Ph.D.[1], Yoshihiro Kanemitsu M.D., Ph.D.[1], Takehiro Uemura M.D., Ph.D.[1], Tomoko Tajiri M.D., Ph.D.[1], Ken Maeno M.D., Ph.D.[1], Yutaka Ito M.D., Ph.D.[1], Tetsuya Oguri M.D., Ph.D.[1], Yoshiyuki Ozawa M.D., Ph.D.[3], Takayuki Murase M.D., Ph.D.[4], and Akio Niimi M.D., Ph.D.[1]

Institutional affiliations:

[1] Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

[2] Department of Respiratory Medicine, Nagoya City University East Medical Center, Nagoya, Japan.

[3] Department of Radiology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

[4] Department of Pathology and Molecular Diagnostics, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan.

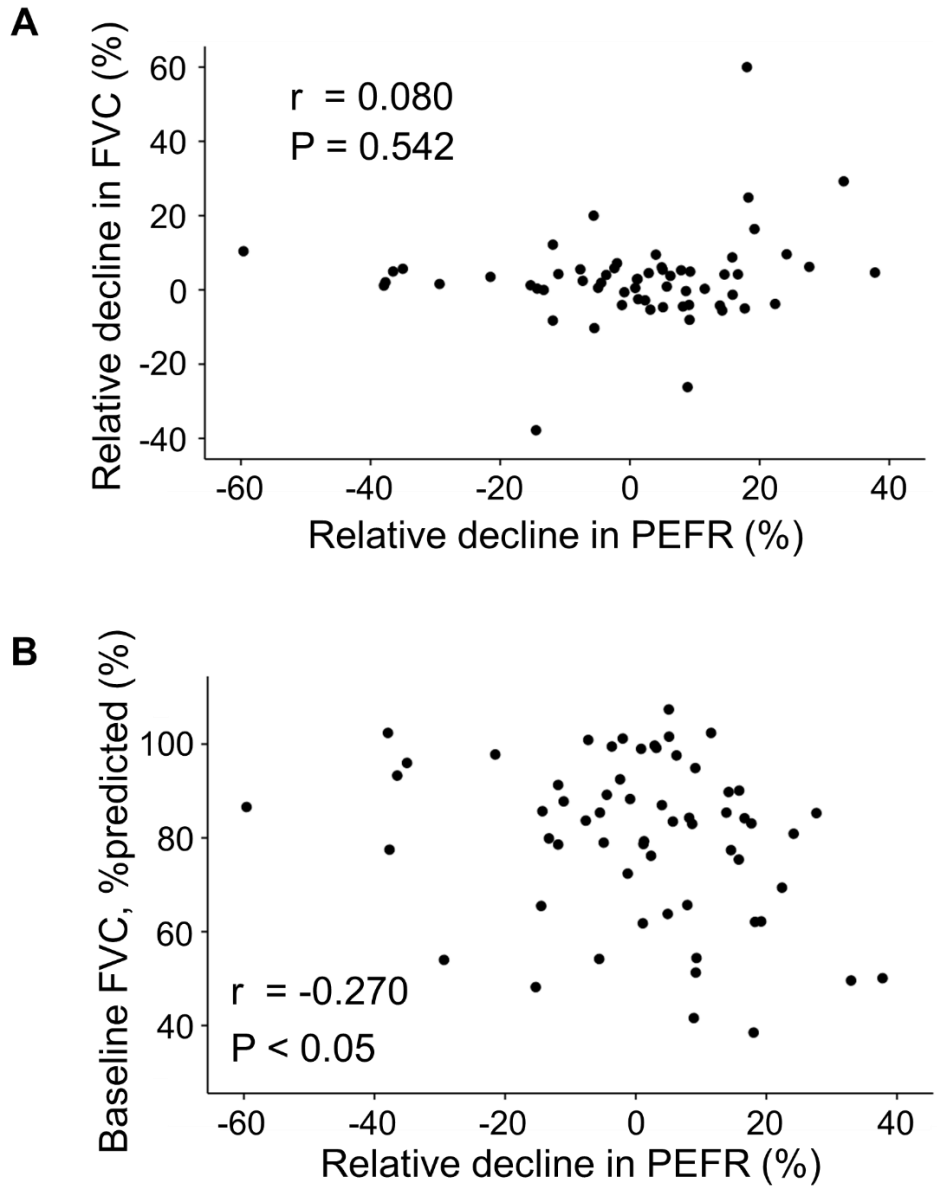
Corresponding author:

Hirotsugu Ohkubo, Department of Respiratory Medicine Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi 467-8601, Japan, **Fax:** +81-52-852-0849, **Phone:** +81-52-853-8216, **E-mail:** hohkubo@med.nagoya-cu.ac.jp

Supplementary Figure S1. Correlations of relative decline in PEFR.

The correlations of relative decline in PEFR with relative decline in FVC (A) and baseline FVC, % predicted (B) are shown.

Abbreviations: PEFR, peak expiratory flow rate; FVC, forced vital capacity.



Supplementary Table S1. Prediction of mortality by univariate and multivariate Cox-proportional hazards analyses in the baseline cohort

Predictor	HR	95%CI	P-value
Univariate analysis			
Age	1.067	0.991 – 1.149	0.085
Sex, female	0.780	0.182 – 3.356	0.739
Body mass index	0.859	0.742 – 0.995	<0.05
Baseline FVC, % predicted	0.941	0.917 – 0.966	<0.001
Baseline PEFR, % predicted	0.978	0.956 – 0.999	0.044
Baseline FEV_1, % predicted	0.947	0.919 – 0.977	<0.001
Baseline MMF, % predicted	1.008	0.995 – 1.020	0.248
Baseline DLco, % predicted	0.973	0.952 – 0.995	<0.05
Baseline ESM_{CSA}, cm^2	1.000	0.999 – 1.000	0.314
Multivariate analysis (Stepwise)			
Baseline FVC, % predicted	0.931	0.905 – 0.959	<0.001

Abbreviations: HR, hazard ratio; CI, confidence interval; FVC, forced vital capacity; PEFR, peak expiratory flow rate; FEV_1, forced expiratory volume in 1.0 second; MMF, maximum mid-expiratory flow rate; DL_{CO}, diffusion capacity of the lung for carbon monoxide; ESM_{CSA}, the cross-sectional area of the erector spinae muscle evaluated using CT images.

Supplementary Table S2. Characteristics of IPF patients separated by the cutoff value of relative decline in PEFR

Variable	Relative decline in PEFR ≥ 8.65%	Relative decline in PEFR < 8.65%	P-value
Total, n	21	40	
Age, y	72.5 ± 8.0	69.0 ± 7.7	0.103
Sex, female, n (%)	2 (9.5%)	5 (12.5%)	0.544
Body mass index, kg/m^2	23.8 ± 3.4	23.6 ± 3.3	0.807
Baseline FVC, % predicted, %	77.4 [54.4 – 85.3]	86.2 [78.3 – 97.7]	<0.05
Baseline PEFR, % predicted, %	72.8 [70.2 – 94.0]	82.5 [70.2 – 90.9]	0.687
Baseline FEV_1, % predicted, %	77.8 [60.1 – 85.3]	85.0 [75.8 – 94.3]	<0.05
Baseline FEV_1/FVC, %	84.4 [78.7 – 91.0]	81.3 [76.8 – 86.5]	0.197
Baseline MMF, % predicted, %	83.1 [60.0 – 115.2]	82.2 [57.0 – 99.8]	0.585
Baseline DL_{CO}, % predicted, %	69.1 [55.1 – 79.2]	75.7 [54.8 – 86.9]	0.276
Baseline ESM_{CSA}, cm^2	29.4 ± 6.5	28.9 ± 6.4	0.827
Observation period, days	717 [498 – 1623]	1133 [702 – 1639]	0.278
Death during observation period, n (%)	12 (57.1%)	9 (22.5%)	<0.01
Relative decline in FVC, %	4.17 [-4.04 – 8.76]	2.26 [-0.15 – 5.33]	0.808
Relative decline in PEFR, %	15.85 [11.54 – 19.22]	-4.04 [-13.54 – 2.49]	<0.001
Relative decline in FEV_1, %	3.17 [-2.40 – 12.08]	3.27 [-1.46 – 8.22]	0.627
Relative decline in MMF, %	6.67 [-12.70 – 15.38]	3.58 [-13.12 – 17.10]	0.940
Pirfenidone treatment, n (%)	15 (71.4%)	26 (65.0%)	0.611
Nintedanib treatment, n (%)	18 (85.7%)	29 (72.5%)	0.201
Corticosteroid treatment, n (%)	4 (19.0%)	9 (22.5%)	0.515
Long-term oxygen therapy, n (%)	12 (57.1%)	14 (35.0%)	0.097
Charlson comorbidity index	2 [1 – 2]	1 [1 – 2]	0.365

Data are presented as means (± standard deviation), medians [interquartile range], or numbers (%).

Abbreviations: PEFR, peak expiratory flow rate; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1.0 second; MMF, maximum mid-expiratory flow rate; DL_{CO}, diffusion capacity of the lung for carbon monoxide; ESM_{CSA}, the cross-sectional area of the erector spinae muscle evaluated using CT images.

Supplementary Table S3. Characteristics of IPF patients with and without anti-fibrotic drugs

Variable	With anti-fibrotic drugs	Without anti-fibrotic drugs	P-value
Total, n	54	7	
Age, y	70.4 ± 8.0	68.7 ± 7.8	0.602
Sex, female, n (%)	7 (13.0%)	0 (0.0%)	0.586
Body mass index, kg/m^2	23.8 ± 3.3	22.6 ± 3.7	0.388
Baseline FVC, % predicted, %	83.1 [65.1 – 92.7]	86.6 [83.5 – 99.0]	0.168
Baseline PEFR, % predicted, %	80.7 [66.6 – 92.9]	82.1 [75.9 – 94.0]	0.868
Baseline FEV_1, % predicted, %	83.3 [77.8 – 87.9]	82.1 [74.0 – 93.3]	0.991
Baseline FEV_1/FVC, %	83.6 [77.8 – 87.9]	75.8 [64.8 – 87.1]	0.083
Baseline MMF, % predicted, %	82.6 [61.1 – 103.6]	52.6 [32.8 – 115.8]	0.457
Baseline DL_{CO}, % predicted, %	71.7 [52.5 – 84.4]	87.9 [73.0 – 99.5]	0.072
Baseline ESM_{CSA}, cm^2	28.6 ± 6.1	32.2 ± 7.7	0.164
Observation period, days	1005 [523 – 1775]	1248 [710 – 1533]	0.698
Death during observation period, n (%)	21 (38.9%)	0 (0.0%)	0.084
Relative decline in FVC, %	2.68 [-3.04 – 5.58]	0.91 [0.35 – 7.20]	1.000
Relative decline in PEFR, %	3.59 [-6.01 – 13.97]	-1.98 [-14.29 – 5.69]	0.190
Relative decline in FEV_1, %	3.18 [-2.44 – 9.17]	3.82 [-5.60 – 9.33]	0.851
Relative decline in MMF, %	2.11 [-13.10 – 16.20]	7.61 [-18.05 – 16.94]	0.868

Data are presented as means (± standard deviation), medians [interquartile range], or numbers (%).

Abbreviations: FVC, forced vital capacity; PEFR, peak expiratory flow rate; FEV_1, forced expiratory volume in 1.0 second; MMF, maximum mid-expiratory flow rate; DL_{CO}, diffusion capacity of the lung for carbon monoxide; ESM_{CSA}, the cross-sectional area of the erector spinae muscle evaluated using CT images.