THE LANCET Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Stuart BD, Lee JS, Kozlitina J, et al. Effect of telomere length on survival in patients with idiopathic pulmonary fibrosis: an observational cohort study with independent validation. *Lancet Respir Med* 2014; published online June 17. http://dx.doi.org/10.1016/S2213-2600(14)70124-9.

Supplemental Table 1. Coding Telomerase Variants Discovered in Sporadic IPF Patients with Telomere Lengths Below the 10th Percentile of Normal (n=38).

Diagnosis	Gene	DNA Change	Predicted Protein Change
IPF	*TERT*	c.2006G>A	R669Q
IPF	*TERT*	c.2593C>T[1]	R865C
IPF	*TERT*	c.2647T>A	F883I
IPF	*TERT*	c.2869A>C[1]	S957R

[1]These individuals were previously described in Tsakiri et. al. 2007, PMID:17460043 and Cronkhite et. al. 2008, PMID:18635888.

Supplemental Table 2. Univariate Survival Analysis of IPF Patients Across All Three Cohorts

	Dallas IPF cohort		Chicago IPF cohort		San Francisco IPF cohort	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Univariate analysis						
Age	1 (0·98 - 1·02)	0·71	0·99 (0·97 - 1·02)	0·68	1·03 (0·99 - 1·07)	0·17
Male Sex	1·42 (0·9 - 2·24)	0.13	1·76 (0·88 - 3·51)	0·11	1·27 (0·49 - 3·31)	0·63
FVC, % predicted	0·75 (0·66 - 0·84)	<0·0001	0·67 (0·55 - 0·81)	<0·0001	0·78 (0·61 - 1·01)	0·057
DL_{CO}, % predicted	0·67 (0·57 - 0·79)	<0·0001	0·61 (0·49 - 0·76)	<0·0001	0·79 (0·61 - 1·02)	0·071
Telomere Length	0·32 (0·14 - 0·72)	0·0058	0·31 (0·11 - 0·84)	0·021	0·38 (0·14 - 1·06)	0·065
GAP score	2·76 (1·9 - 4·01)	<0·0001	3·49 (1·89 - 6·42)	<0·0001	2·72 (1·29 - 5·74)	0·0084

The reported hazard ratios are for a 1-year difference in age, a 10% difference in FVC and DL_{CO} measurements, and a 1-unit difference in log T/S ratio and GAP score. Data for FVC or DL_{CO} (or both) were unavailable for some patients. The univariate analysis included all patients with available data (as shown in Table 1). Patients who were unable to do the DL_{CO} test (eight in the Dallas cohort, one in the Chicago cohort, and one in the San Francisco cohort) were included in the analysis using the GAP score. IPF=idiopathic pulmonary fibrosis. HR=hazard ratio. FVC=forced vital capacity. DL_{CO}=diffusion capacity for carbon monoxide. GAP=gender-age-physiology.

Supplemental Table 3. Univariate Analysis of Transplant-free Survival of Non-IPF ILD Patients in the Dallas Cohort.

	Dallas non-IPF cohort	
	HR (95% CI)	P-value
Univariate analysis		
Age	1·03 (1 - 1·05)	0·022
Male Sex	1·81 (1·05 – 3·12)	0·033
FVC, % predicted	0·8 (0·7 - 0·92)	0·0015
DL_{CO}, % predicted	0·51 (0·39 - 0·67)	<0·001
Telomere Length	0·72 (0·23 - 2·23)	0·57

The reported hazard ratios are for a 1-year difference in age, a 10% difference in FVC and DL_{CO} measurements, and a 1-unit difference in log T/S ratio and GAP score. Data for DL_{CO} was unavailable for some patients. The univariate analysis included all patients with available data (as shown in Table 1). IPF=idiopathic pulmonary fibrosis. ILD=interstitial lung disease. HR=hazard ratio. FVC=forced vital capacity. DL_{CO}=diffusion capacity for carbon monoxide.

Supplemental Table 4. Sensitivity Analyses for Survival of IPF Patients Across Three Cohorts (with Censoring of Lung Transplantation Events).

	Dallas IPF cohort		**Chicago IPF cohort**		**San Francisco IPF cohort**	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Univariate analysis						
Age	1·02 (1·00 - 1·04)	0·099	1·00 (0·97 - 1·03)	0·94	1·06 (1·01 - 1·11)	0·015
Male sex	1·18 (0·72 - 1·94)	0·5	1·6 (0·8 - 3·21)	0·19	1·06 (0·4 - 2·83)	0·90
FVC, % predicted	0·79 (0·7 - 0·9)	<0·0001	0·65 (0·53 - 0·8)	<0·0001	0·80 (0·61 - 1·06)	0·12
DL_{CO}, % predicted	0·63 (0·52 - 0·77)	<0·0001	0·65 (0·52 - 0·80)	0·00010	0·79 (0·59 - 1·05)	0·10
Telomere Length	0·34 (0·14 - 0·85)	0·021	0·27 (0·09 - 0·75)	0·012	0·27 (0·09 - 0·82)	0·021
GAP score	3·4 (2·2 - 5·26)	<0·0001	3·58 (1·89 - 6·78)	<0·0001	3·61 (1·51 - 8·61)	0·0038
Multivariable analysis (individual covariates)	(n=135)		(n=123)		(n=49)	
Age	1·03 (1·00 - 1·07)	0·040	1·00 (0·97 - 1·04)	0·90	1·06 (1·00 - 1·12)	0·034
Male sex	1·23 (0·7 - 2·13)	0·47	1·92 (0·75 - 4·88)	0·17	1·02 (0·28 - 3·80)	0·97
FVC, % predicted	0·89 (0·72 - 1·09)	0·24	0·81 (0·62 - 1·06)	0·13	0·90 (0·66 - 1·24)	0·53
DL_{CO}, % predicted	0·63 (0·49 - 0·8)	0·00017	0·66 (0·51 - 0·86)	0·0022	0·73 (0·52 - 1·01)	0·061
Telomere Length	0·35 (0·11 - 1·15)	0·085	0·11 (0·03 - 0·41)	0·0011	0·13 (0·03 - 0·52)	0·0040
Multivariable analysis (GAP score)	(n=143)		(n=124)		(n=50)	
GAP score	3·27 (2·1 – 5·1)	<0·0001	3·8 (1·94 - 7·42)	<0·0001	3·81 (1·62 - 8·97)	0·0022
Telomere length	0·6 (0·21 - 1·76)	0·35	0·2 (0·05 - 0·74)	0·016	0·14 (0·03 - 0·53)	0·0041

The reported hazard ratios are per a 1-year difference in age, a 10% difference in FVC and DL_{CO} measurements, and a 1-unit difference in log T/S ratio and GAP score. Data for FVC or DL_{CO} (or both) were unavailable for some patients. The univariate analysis included all patients with available data (as shown in Table 1). Patients who were unable to do the DL_{CO} test (eight in the Dallas cohort, one in the Chicago cohort, and one in the San Francisco cohort) were excluded from the multivariable analysis when using individual covariates, but included when using the GAP score. IPF=idiopathic pulmonary fibrosis. HR=hazard ratio. FVC=forced vital capacity. DL_{CO}=diffusion capacity for carbon monoxide. GAP=gender-age-physiology.