

Figure E1: A) Calibration of the Distance-Oxygen-Gender-Age-Physiology (DO-GAP) index in the internal cohort B) Calibration of the DO-GAP index in the external cohort. Smoothed pseudovalues (dashed lines) with pointwise 95% confidence intervals (shaded area) are plotted against predicted event probabilities at 2 years of follow-up. The solid line is the line of identity, denoting perfect calibration. Tables beneath the figures are the results of statistical tests of overall model calibration over multiple time points (yearly over 3 years of follow-up) where the null hypothesis assumes the intercept equal to 0 and the slope of the model equal to 1.

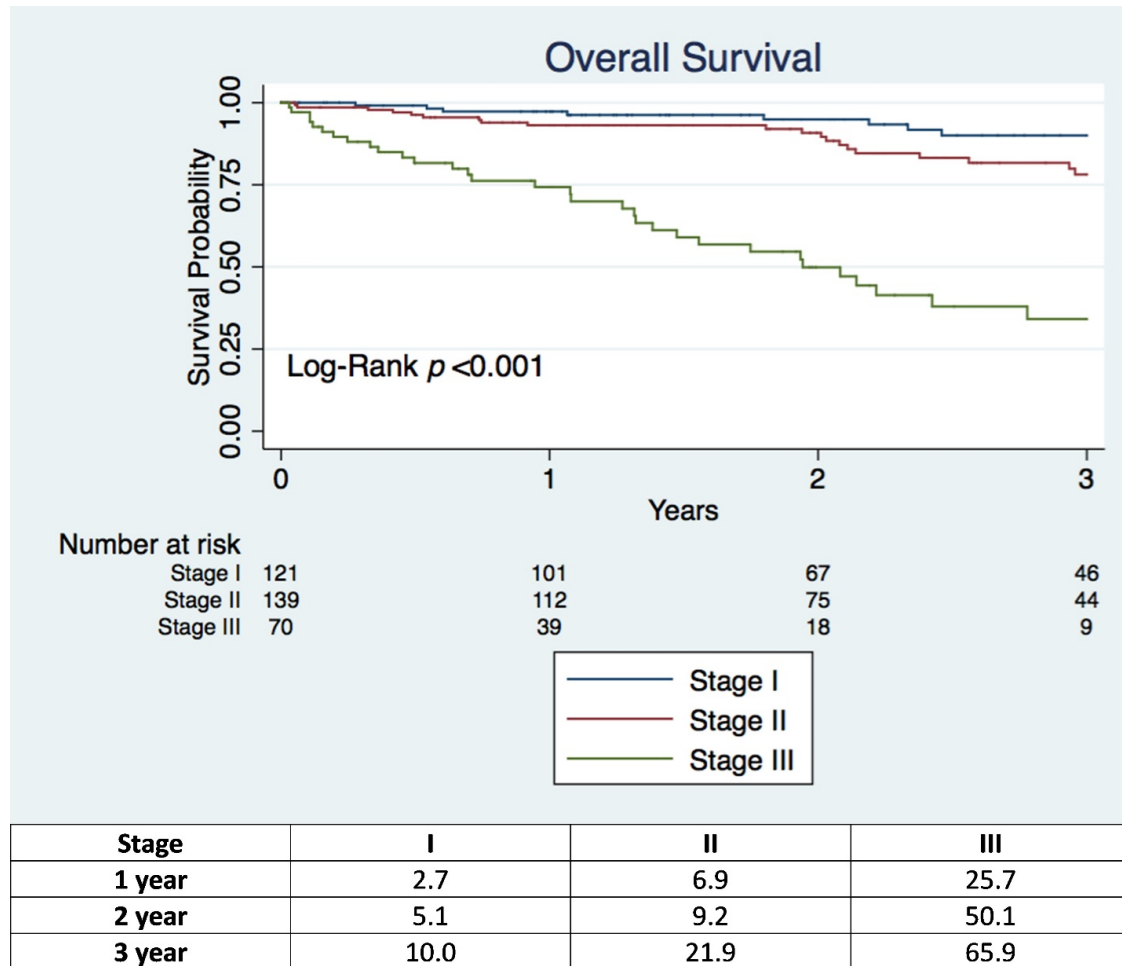


Figure E2: Kaplan-Meier survival curves for patients treated with antifibrotic therapy from time of initial pulmonary function testing based on idiopathic pulmonary fibrosis stage as defined by the proposed distance-oxygen-gender-age-physiology (DO-GAP) index. Table beneath figure includes the estimated observed overall mortality (%) by DO-GAP stage based on patients on antifibrotic therapy in the entire cohort.

Table E1. Refit GAP index constructed utilizing the pre-specified categorical assignments from the original GAP index and linear rescaling of the regression coefficients in the derivation set.

Predictor	Category	Points
Gender	Female	0
	Male	1
Age (years)	≤60	0
	61-65	2
	>65	5
Physiology	FVC, % predicted	
	>75	0
	50-75	11
	<50	18
	DLCO, % predicted	
	>55	0
	36-55	12
	≤35	25
	Cannot perform	25

Table E2. Change in classified stage in the validation set based on application of the DO-GAP index staging system compared to the original GAP index staging system

GAP Stage	Patients (N)	DO-GAP Stage (N)			Percent reclassified (%)
		I	II	III	
I	52	42	9	1	19.2
II	136	42	79	15	41.9
III	93	0	20	73	21.5
Overall	281	84	108	89	31.0

GAP, gender-age-physiology; DO-GAP, distance-oxygen-gender-age-physiology

Table E3. Sensitivity analysis in the derivation set of the association of predictors with mortality in patients with idiopathic pulmonary fibrosis treating lung transplantation as a competing risk of death

Variables	Univariate analysis		Multivariable analysis	
	SHR (95% CI)	P-value	SHR (95% CI)	P-value
GAP index	1.48 (1.27-1.72)	<0.001	1.22 (1.05-1.43)	0.011
Exertional hypoxia	3.56 (2.28-5.55)	<0.001	2.31 (1.39-3.83)	0.001
6MWD <250m	4.55 (2.90-7.13)	<0.001	2.73 (1.62-4.60)	<0.001

SHR, subdistribution hazard ratio; 6MWD, six-minute walk distance

Table E4. Sub-group analysis comparing the added discriminative value of the DO-GAP index compared to the GAP index in patients on antifibrotic therapy

Model	C-statistic (95% CI)	Difference in C-statistic compared to refit GAP		NRI (%) (95% CI) ^a	IDI _{event} (95% CI) ^a	IDI _{non-event} (95% CI) ^a	IDI ^a
		Difference (95% CI)	P-value				
GAP index	0.696 (0.595-0.796)	0.002 (-0.038-0.041)	0.929	-12.5 (-55.8-45.2)	0.003 (-0.010-0.040)	0.000 (-0.001-0.005)	-0.003 (-0.011-0.045)
Refit GAP index	0.694 (0.599-0.788)	-	-	-	-	-	-
DO-GAP index	0.755 (0.665-0.844)	0.061 (-0.013-0.135)	0.104	42.8 (3.5-83.3)	0.060 (0.007-0.160)	0.006 (0.001-0.018)	0.066 (0.007-0.178)

NRI, net reclassification improvement; IDI, incremental discrimination improvement; GAP, gender-age-physiology; DO-GAP, distance-oxygen-gender-age-physiology

^aImprovement comparisons made to the GAP index after refitting original GAP index to the derivation set

Table E5. Sub-group analysis comparing the added discriminative value of the DO-GAP index compared to the GAP index in patients evaluated within 5 years of study completion

Model	C-statistic (95% CI)	Difference in C-statistic compared to refit GAP		NRI (%) (95% CI) ^a	IDI _{event} (95% CI) ^a	IDI _{non-event} (95% CI) ^a	IDI
		Difference (95% CI)	P-value				
GAP index	0.758 (0.661-0.855)	-0.005 (-0.045-0.035)	0.807	9.7 (-50.0, 44.0)	0.008 (-0.012-0.070)	0.000 (-0.002-0.012)	0.008 (-0.014-0.082)
Refit GAP index	0.763 (0.674-0.852)	-	-	-	-	-	-
DO-GAP index	0.806 (0.729-0.883)	0.043 (-0.028-0.114)	0.232	31.8 (16.0-74.8)	0.050 (0.001-0.125)	0.008 (0.001-0.022)	0.058 (0.002-0.143)

NRI, net reclassification improvement; IDI, incremental discrimination improvement; GAP, gender-age-physiology; DO-GAP, distance-oxygen-gender-age-physiology

^aImprovement comparisons made to the GAP index after refitting original GAP index to the derivation set