SUPPLEMENTAL MATERIAL

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Introducing a new prognostic instrument for long-term mortality prediction in COPD patients: the CADOT index (doi: 10.5507/bp.2020.035)

Table A1. ROC analysis – parameter/index capacity to identify patients with mortality risk.

	C-statistics (95% CI)	*P*	De Long test	
			Difference	*P*
BODE	0.677 (0.610; 0.744)	**<0.001**	-	-
ADO	0.644 (0.581; 0.706)	**<0.001**	-	-
Adding to BODE				
CHF	0.702 (0.634; 0.770)	**<0.001**	0.025	0.186
FEV_1/FVC (%)	0.682 (0.618; 0.747)	**<0.001**	0.005	0.405
TL_{CO} (%)	0.728 (0.657; 0.798)	**<0.001**	0.051	0.182
K_{CO} (%)	0.744 (0.677; 0.810)	**<0.001**	0.067	0.087
Adding to ADO				
CHF	0.689 (0.630; 0.748)	**<0.001**	0.045	**0.022**
FEV_1/FVC (%)	0.652 (0.589; 0.715)	**<0.001**	0.008	0.477
TL_{CO} (%)	0.705 (0.634; 0.776)	**<0.001**	0.061	**0.006**
K_{CO} (%)	0.693 (0.617; 0.769)	**<0.001**	0.049	**0.015**

ADO = Age, Dyspnoea and airflow Obs"truction; BODE = Body-mass index, airflow Obstruction, Dyspnoea, and Exercise; CHF = chronic heart failure; CI = Confident Interval; FEV_1 = Forced Expiratory Volume in 1 Second; FVC = Forced Vital Capacity; K_{CO} = Transfer Coefficient for Carbon Monoxide; TL_{CO} = Diffusing Capacity for Carbon Monoxide

Table A2. Development of the new index (ADO + CHF, TL_{CO}, K_{CO}) by reclassification analysis.

	cfNRI (95% CI)	*P*	IDI (95% CI)	*P*
CHF	37.06 (15.92; 58.19)	**<0.001**	0.015 (0.001; 0.028)	**0.032**
TL_{CO} (%)	43.73 (14.66; 72.81)	**0.003**	0.027 (0.004; 0.051)	**0.023**
K_{CO} (%)	12.56 (-17.85; 42.98)	0.418	0.014 (-0.007; 0.034)	0.184

ADO = Age, Dyspnoea and airflow Obstruction; CHF = Heart failure CI = Confident Interval; cfNRI = Category Free Net Reclassification Improvement; IDI = Integrated Discrimination Improvement; K_{CO} = Transfer Coefficient for Carbon Monoxide; TL_{CO} = Diffusing Capacity for Carbon Monoxide

Table A3. Distribution of patients from the derivation and validation cohorts according to the CADOT total scores.

	Derivation cohort – CZ		Validation cohort – NL	
	n (%)	Risk group	n (%)	Risk group
0	0 (0.0%)	Low risk (n=20; 4.4%)	1 (0.5%)	Low risk (n=35; 19.0%)
1	3 (0.7%)		9 (4.9%)	
2	17 (3.7%)		25 (13.6%)	
3	52 (11.3%)	Intermediate risk (n=212; 46.2%)	39 (21.2%)	Intermediate risk (n=111; 60.3%)
4	83 (18.1%)		44 (23.9%)	
5	77 (16.8%)		28 (15.2%)	
6	59 (12.9%)	High risk (n=197; 42.9%)	24 (13.0%)	High risk (n=38; 20.7%)
7	44 (9.6%)		8 (4.3%)	
8	58 (12.6%)		4 (2.2%)	
9	36 (7.8%)		2 (1.1%)	
10	15 (3.3%)	Very high risk (n=30; 6.5%)	0 (0.0%)	Very high risk (n=0; 0.0%)
> 10	15 (3.3%)		0 (0.0%)	

CZ – Czech Republic; NL - Netherlands

Table A4. Descriptive statistics of the validation cohort (n=187).

	Total	Death		*P*
		No	Yes	
Sex – men (n, %)	110 (58.8%)	99 (57.9%)	11 (68.8%)	0.440
Age		N=171	N=16	**<0.001**
(median, 5th; 95th percentile)	64.0 (51.0; 75.0)	63.0 (51.0; 75.0)	70.0 (60.0; 77.0)	
BMI		N=170	N=16	0.466
(median, 5th; 95th percentile)	25.9 (19.2; 35.1)	25.9 (19.3; 35.1)	25.2 (16.7; 33.2)	
mMRC (n, %)				
0	24 (13.0%)	22 (13.0%)	2 (12.5%)	**0.034**
1	59 (31.9%)	58 (34.3%)	1 (6.3%)	
2	83 (44.9%)	74 (43.8%)	9 (56.3%)	
3	11 (5.9%)	9 (5.3%)	2 (12.5%)	
4	8 (4.3%)	6 (3.6%)	2 (12.5%)	
GOLD (n, %)				
I	7 (3.8%)	7 (4.2%)	0 (0.0%)	0.402
II	81 (44.3%)	77 (45.8%)	4 (26.7%)	
III	69 (37.7%)	61 (36.3%)	8 (53.3%)	
IV	26 (14.2%)	23 (13.7%)	3 (20.0%)	
6MWD (m)		n=169	n=16	**<0.001**
(median, 5th; 95th percentile)	510.0 (340.0; 657.0)	522.0 (353.0; 658.0)	383.5 (223.0; 572.0)	
FEV_1 (l)		n=171	n=16	**0.016**
(median, 5th; 95th percentile)	1.4 (0.6; 2.5)	1.4 (0.7; 2.5)	1.0 (0.5; 2.1)	
FEV_1 (%)		n=171	n=16	**0.015**
(median, 5th; 95th percentile)	50.0 (26.0; 80.0)	51.0 (26.0; 81.0)	34.0 (22.0; 75.0)	
FEV_1/FVC	0.51 (0.31; 0.79)	n=171	n=16	0.233
(median, 5th; 95th percentile)		0.51 (0.31; 0.81)	0.46 (0.31; 0.72)	
FVC in (l)	3.3 (1.9; 5.3)	n=171	n=16	0.073
(median, 5th; 95th percentile)		3.3 (2.1; 5.4)	2.8 (1.8; 4.4)	
FVC in (%)	95.0 (65.0; 130.0)	n=171	n=16	**0.013**
(median, 5th; 95th percentile)		97.0 (65.0; 130.0)	89.0 (63.0; 111.0)	
FVC (l)	3.3 (2.0; 5.5)	n=171	n=16	**0.032**
(median, 5th; 95th percentile)		3.4 (2.0; 5.6)	2.7 (1.9; 4.5)	
FVC (%)	100.0 (67.0; 134.0)	n=171	n=16	**0.008**
(median, 5th; 95th percentile)		103.0 (68.0; 134.0)	93.0 (55.0; 116.0)	
RV (l)	3.5 (2.2; 5.6)	n=169	n=16	**0.010**
(median, 5th; 95th percentile)		3.4 (2.2; 5.5)	4.3 (2.7; 6.2)	
RV (%)	156.0 (98.0; 234.0)	n=169	n=16	0.079
(median, 5th; 95th percentile)		154.0 (96.0; 230.0)	186.0 (110.0; 277.0)	
TLC (l)	6.9 (5.0; 9.7)	n=170	n=16	0.586
(median, 5th; 95th percentile)		6.9 (5.0; 9.8)	7.4 (4.7; 9.4)	
TLC (%)		n=170	n=16	0.940
(median, 5th; 95th percentile)	120.0 (91.0; 144.0)	120.0 (91.0; 144.0)	124.0 (90.0; 156.0)	
TL_{CO} (mmol/min/kPa)	4.6 (2.5; 7.4)	n=171	n=16	**0.018**
(median, 5th; 95th percentile)		4.6 (2.5; 7.4)	3.6 (1.8; 6.8)	
TL_{CO} (%)	56.0 (31.0; 80.0)	n=171	n=16	**0.034**
(median, 5th; 95th percentile)		56.0 (33.0; 80.0)	42.5 (25.0; 80.0)	
K_{CO} (mmol/min/kPa)	0.9 (0.5; 1.5)	n=171	n=16	0.175
(median, 5th; 95th percentile)		1.0 (0.6; 1.5)	0.9 (0.4; 1.8)	
K_{CO} (%)	65.0 (38.0; 102.0)	n=171	n=16	0.610
(median, 5th; 95th percentile)		65.0 (39.0; 102.0)	62.0 (32.0; 125.0)	

Table A4. *(Continued)*

	Total	Death		*P*
		No	Yes	
Charlson comorbidity index (n, %)				
Myocardial infarction	20 (10.8%)	18 (10.6%)	2 (12.5%)	0.684
Heart Failure	5 (2.7%)	4 (2.4%)	1 (6.3%)	0.365
Peripheral vascular disease	31 (16.7%)	28 (16.5%)	3 (18.8%)	0.733
Cerebrovascular disease	17 (9.1%)	16 (9.4%)	1 (6.3%)	0.999
Dementia	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
COPD	185 (99.5%)	169 (99.4%)	16 (100.0%)	0.999
Connective tissue disease	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Ulcer disease	12 (6.5%)	10 (5.9%)	2 (12.5%)	0.276
Mild liver disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Diabetes mellitus	11 (5.9%)	9 (5.3%)	2 (12.5%)	0.242
Hemiplegia	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Renal disease	2 (1.1%)	1 (0.6%)	1 (6.3%)	0.165
Diabetes end organ damage	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Tumour	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Leukaemia	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Lymphoma	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Moderate or several liver disease	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.999
Metastatic malignancy	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
AIDS	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Score (n, %)				
0	1 (0.5%)	1 (0.6%)	0 (0.0%)	0.126
1	112 (60.2%)	104 (61.2%)	8 (50.0%)	
2	45 (24.2%)	38 (22.4%)	7 (43.8%)	
3	22 (11.8%)	22 (12.9%)	0 (0.0%)	
4	3 (1.6%)	3 (1.8%)	0 (0.0%)	
5	2 (1.1%)	1 (0.6%)	1 (6.3%)	
6	1 (0.5%)	1 (0.6%)	0 (0.0%)	
BODE		n=167	n=16	**<0.001**
(median, 5th; 95th percentile,	2.0 (0.0; 5.0)	2.0 (0.0; 5.0)	4.0 (0.0; 6.0)	
mean, SD)	2.4 (1.6)	2.2 (1.5)	3.9 (1.5)	
ADO		n=169	n=16	**<0.001**
(median, 5th; 95th percentile,	4.0 (1.0; 6.0)	3.0 (1.0; 6.0)	5.0 (3.0; 8.0)	
mean, SD)	3.6 (1.4)	3.5 (1.4)	5.1 (1.2)	

6-MWD = Six Minute Walking Distance; ADO = Age, Dyspnoea and airflow Obstruction; BMI = Body Mass Index; BODE = Body-mass index, airflow Obstruction, Dyspnoea, and Exercise; FEV_1 = Forced Expiratory Volume in 1 Second; FVC = Forced Vital Capacity; K_{CO} = Transfer Coefficient for Carbon Monoxide; mMRC = modified Medical Research Council dyspnoea scale; RV = residual volume; TLC = total lung capacity; TL_{CO} = diffusing capacity (Transfer Factor) for Carbon Monoxide

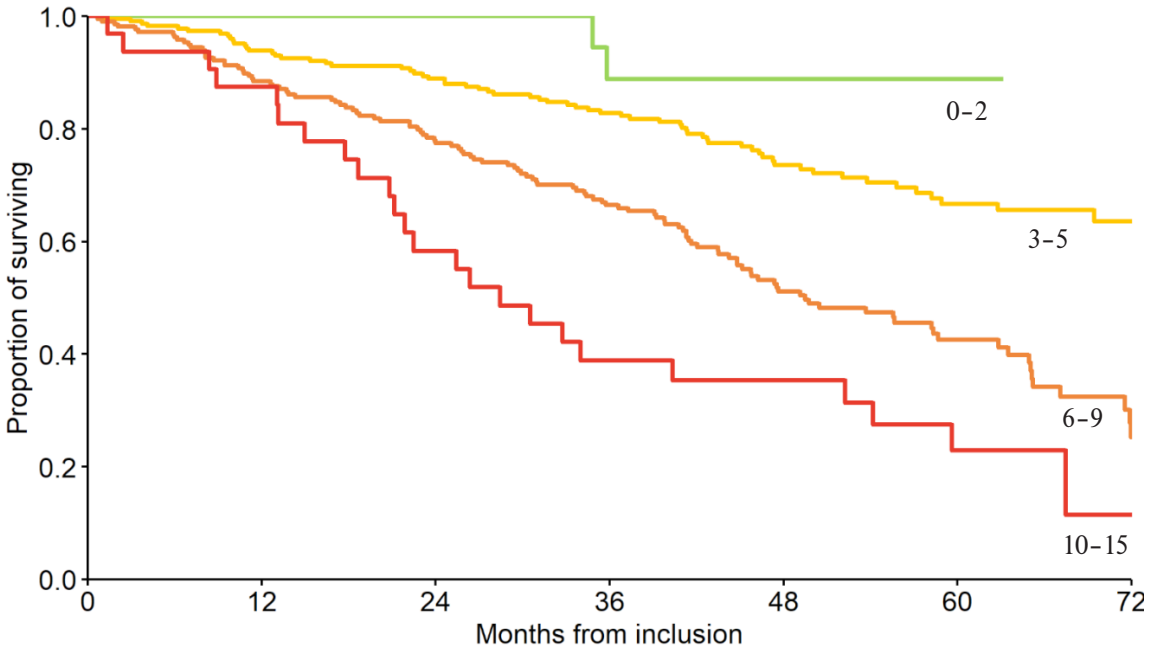

Fig. A1. Long-term survival according to the CADOT index (re-assessment with the 2020 CMRD data export).

CADOT score	Median of survival (95%CI)	Survival probability (95%CI)					Log Rank (*P*)	HR (95% CI)
		12 months	24 months	36 months	48 months	60 months		
0–2	-	1 (1–1)	1 (1–1)	0.889 (0.755–1)	0.889 (0.755–1)	0.889 (0.755–1)	**<0.001**	Reference category
3–5	-	0.939 (0.908–0.97)	0.889 (0.849–0.931)	0.828 (0.779–0.879)	0.736 (0.677–0.8)	0.667 (0.599–0.743)		2.684 (0.656–10.975)
6–9	49.5 (40.4–58.6)	0.885 (0.843–0.928)	0.775 (0.721–0.833)	0.665 (0.603–0.732)	0.511 (0.443–0.589)	0.426 (0.355–0.511)		6.372 (1.574–25.794)*
10–15	28.4 (18.5–38.4)	0.875 (0.768–0.997)	0.583 (0.433–0.785)	0.389 (0.250–0.605)	0.354 (0.219–0.571)	0.229 (0.115–0.458)		11.572 (2.739–48.892)*

* Statistically significant difference in HR compared to the reference category