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Phenotypic Characteristics of Patients With Chronic Obstructive Pulmonary Disease After Stratification for the Short Physical Performance Battery Summary Score Peer-reviewed author version

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RUNNING HEAD: Mobility and balance in COPD.

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CORRESPONDENCE TO: Anouk A.F. Stoffels, MSc, Department of Pulmonary diseases, Dekkerswald Radboudumc, Nijmegen, the Netherlands; e-mail: anouk.stoffels@radboudumc.nl. TITLE: Phenotypic characteristics of patients with Chronic Obstructive Pulmonary
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3

4 ABSTRACT

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Objective: To assess the phenotypic characteristics of patients with Chronic Obstructive
Pulmonary Disease (COPD) after stratification for Short Physical Performance Battery (SPPB)
summary scores and to determine phenotypic characteristics of the SPPB summary score at the
start of pulmonary rehabilitation (PR).
Design: Retrospective, cross-sectional.

11 **Setting:** Baseline assessment for PR program.

Participants: 900 patients with COPD (age 65±8 years, 52% male, FEV₁ 43 (31-62)%
predicted).

14 Interventions: Not applicable.

Main outcome measure: Patients were stratified according to their SPPB summary scores into low-performance (LP), moderate-performance (MP) or high-performance (HP). Furthermore, lung function, arterial blood gases, body composition, physical capacity, lower-limb muscle strength and endurance and symptoms of anxiety and depression were assessed.

19 Results: Generally, physical capacity and muscle function were lower and scores for symptoms 20 of anxiety and depression were higher in LP patients compared to MP and HP patients (all 21 values, p<0.01). However, 25% of HP patients with COPD scored high on symptoms of anxiety 22 and/or depression (≥10 points) and HP patients still had on average an impaired physical 23 capacity (median 6 minute walk test distance (6MWD) distance of 68% predicted). 24 Furthermore, age and 6MWD (meters) were the only independent predictors in a multivariate 25 regression model, explaining 29% of the variance in SPPB summary score.

26	Conclusions: In COPD, LP patients have the worst physical and emotional functioning.
27	However, HP patients can still exhibit physical and emotional impairments. As the explained
28	variance in SPPB summary score is low, SPPB should not be considered as a test to discriminate
29	between patients with COPD with a low or preserved physical capacity and emotional status.
30	
31	Keywords: Pulmonary Disease, Chronic Obstructive; Anxiety; Depression; Postural Balance;
32	Physical Fitness; Physical Functional Performance
33	
34	ABBREVIATIONS: CAT = COPD Assessment Test; COPD = chronic obstructive pulmonary
35	disease; CWRT = constant work rate test; FFM = fat free mass; HP = high-performance; LP =
36	low-performance; MP = moderate-performance; PR = pulmonary rehabilitation; SPPB = short
37	physical performance battery; Wmax = maximal workload; 4MGS = four meter gait speed;
38	5STS = five-repetition sit-to-stand; $6MWT = 6$ minute walk test

Airflow limitation is a cardinal feature of patients with chronic obstructive pulmonary disease (COPD)¹. Additionally, evidence shows extra-pulmonary consequences like impairment in balance control and mobility²⁻⁴, which are mainly caused by lower-limb muscle weakness⁵. Mobility and balance deficits may induce more falls⁶ and provoke difficulties in performing activities of daily living safely and independently⁷⁻⁹. Furthermore, it can be the first sign of further functional decline and, therefore, it is important to identify patients with COPD with reduced balance and mobility to prevent disability in activities of daily living¹⁰⁻¹².

The Short Physical Performance Battery (SPPB) is a commonly used, simple and quick 47 performance measure to evaluate mobility and balance, and is recommended in older patients 48 by the European Medicines Agency¹³. Furthermore, the SPPB score has prognostic value as it 49 might identify a subsequent decline in activities of daily living status, rehospitalization and 50 mortality in elderly, including COPD, after hospital discharge ¹⁴. Individuals can be grouped 51 52 based on their SPPB summary score into a low-performance (LP), a moderate-performance (MP), and a high-performance (HP) group¹¹. Patel *et al.* and Mohan *et al.* were the first to 53 evaluate the physical phenotypic characteristics of the abovementioned SPPB performance 54 groups in patients with COPD^{15,16}. Indeed, LP patients with COPD had more functional 55 impairment, loss of muscle mass and structural muscle abnormality compared to HP patients¹⁵. 56 57 Furthermore, a longer 6-minute walk test (6MWT) distance, greater quadriceps maximal voluntary contraction strength, lower age, self-reported hypertension and dyspnea, and being 58 married decreased the likelihood of being in the LP group¹⁶. These data need further 59 corroboration in a non-UK-based settings, as geographic differences in clinical characteristics 60 and management of COPD are known¹⁷. 61

52 Symptoms of anxiety and depression are also common in patients with COPD¹⁸, and 53 significantly correlate with mobility and balance in healthy elderly^{19,20}. However, it remains 54 unclear whether and to what extent a similar pattern occurs in emotional status (i.e. symptoms of anxiety and depression) after stratification for SPPB summary scores. Furthermore, it is
unclear whether and to what extent physical and emotional impairment is also present in HP
patients. This is important to know, as HP patients may give a first impression that they have a
normal physical and emotional functioning.

69 The current study aimed to assess phenotypic characteristics of patients with COPD after 70 stratification for SPPB summary scores and to investigate which phenotypic characteristics 71 determine the SPPB summary score at the start of pulmonary rehabilitation (PR).

72

73 **METHODS**

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75 This retrospective analysis of an observational, cross-sectional study included anonymized data of 953 patients, evaluated during baseline assessment of a comprehensive PR between January 76 2016 and January 2018 in a specialized PR clinic. All measurements were performed by a 77 highly-trained and skilled team of biomedical engineers and laboratory technicians. The 78 medical ethical committee informed the authors that the Medical Research Involving Human 79 Subjects Act (WMO) does not apply to this retrospective study using de-identified, pre-existing 80 data and that an official approval of this study by our committee is not required (METC 2018-81 0541). This study was conformed to the principles of the Declaration of Helsinke. 82

Inclusion criteria were a primary diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria¹ and complete data available regarding SPPB. This latter may result in selection bias. Furthermore, patients were excluded from this analysis if they participated in the PR program for the second time during the inclusion period and/or if they were younger than 40 years of age.

88

89 **Baseline characteristics**

Age, gender, weight, body mass index, the degree of dyspnea (modified Medical Research Council; mMRC²¹), health status (COPD Assessment Test; CAT²²), exacerbation and all-cause hospitalization frequency in the last 12 months, Charlson Comorbidity Index²³ and use of longterm oxygen therapy were systematically assessed. A mMRC dyspnea grade of $\geq 2^1$, CAT score of ≥ 10 and ≥ 18 points^{24,25} were used to classify patients as highly symptomatic.

95

96 Short Physical Performance Battery

Patients performed the SPPB according to the National Institute on Aging protocol²⁶. Firstly, the standing balance measurement was performed in which the patient is required to maintain three stances for 10 seconds (feet placed side-by-side, semi-tandem and tandem). The four meter gait speed (4MGS) test assessed the time needed to walk four meter at habitual gait speed from a standing position. This test was performed twice and the best time was used to score the test. In the five-repetition sit-to-stand test (5STS), the time was measured to complete five sitto-stand maneuvers as quick as possible with arms folded in front of their chest.

Each component was scored from 0 (mobility impairment) to 4 points (no mobility impairment),
resulting in a SPPB summary score ranging from 0 to 12 points. The scoring system can be
found in e-Table 1. Additionally, patients were classified as LP (0-6 points), MP (7-9 points)
or HP (10-12 points)¹¹.

108

109 Phenotypic characteristics

The GOLD classification²⁷ and arterial blood gases were evaluated. Furthermore, spirometry,
 static lung volumes and transfer factor for carbon monoxide by single-breath method were
 executed according to the European Respiratory Society recommendations²⁸ (MasterScreen
 PFT/ Body^a).

Waist circumference was measured and fat-free mass (FFM) and T-scores of the hip 114 115 (trochanter) and lumbar spine (L2-L4) were evaluated using dual energy x-ray absorptiometry (DEXA) (Lunar iDXA^b)²⁹. The FFM index was calculated by dividing FFM by height*height. 116 The reference values of International Diabetes Federation were used for waist circumference³⁰. 117 Physical capacity was assessed using the 6 minute walk test (6MWT), maximal incremental 118 cardiopulmonary exercise test and constant work rate test (CWRT). The 6MWT was performed 119 indoor, on a flat and straight walking course of 30 meters, following the ERS/ATS 120 guidelines^{31,32}. Reference values from Troosters et al.³³ were used and a cutoff value of 350 121 meters according to Spruit et al. was applied to predict respiratory related hospitalization³⁴. The 122 123 maximal cardiopulmonary exercise test was performed on an electromagnetically braked cycle ergometer (Ergoselect^c) according to the recommended guidelines³⁵. The maximal workload 124 (Wmax) was calculated as a percentage of the predicted value³⁶. The CWRT was performed on 125 126 the same ergometer at 75% of the predetermined Wmax. Patients cycled until symptom limitation or until pedaling rate decreased under 60 rpm (with a maximum of 20 minutes)³⁷. 127

Isotonic muscle strength was measured by one repetition-maximum leg press, leg extension, upper back and chest press using standard weight training apparatus (Technogym^d) and was corrected for the FFM of the legs or arms. Isokinetic quadriceps peak torque (Nm) and endurance (total amount of delivered work, J) of the right leg were assessed with a computerized dynamometer (Biodex Multi-joint System 3^e) and also corrected for the FFM of the legs. Patients performed a set of 30 repetitions at an angular speed of 90°/s.

The Hospital Anxiety and Depression Scale was used as a screening tool to detect symptoms
of anxiety and depression. A cutoff point of >10 points was used for each domain³⁸.

136

137 Statistical analyses

Statistical analyses were performed using SPSS, version 25.0^f. Descriptive data were presented 138 139 as mean \pm SD, median (interquartile) or percentages, as appropriate. Differences between included and excluded patients were tested by an unpaired t-test or Mann-Whitney U test as 140 appropriate. Differences between LP, MP and HP groups were tested by one-way analysis of 141 variance (ANOVA) or Kruskal-Wallis test as appropriate. Categorical data were tested with a 142 Chi-square test. When a statistically significant difference was obtained, a pairwise post-hoc 143 test was performed and Bonferroni post-hoc testing was applied to correct for multiple 144 comparison. Due to the many statistical tests performed in this study, a p-value <0.01 was 145 considered significant. 146

Univariate and multivariate regression models were used to assess the associations between the phenotypic characteristics and the SPPB summary score, both using the ENTER method. Explanatory variables, based on univariate models, with a p-value <0.20 and not highly correlated with another variable of interest were used to build the multivariate linear regression model. Variables with a p-value <0.05 were considered as independent predictors of SPPB summary score.

153

154 **RESULTS**

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Nine hundred of the 953 patients with COPD were analysed. Reasons for exclusion were absence of SPPB data (n=1), being younger than 40 years (n=5), participating in the PR program for the second time (n=20), and erroneous download from the database (n=27). Differences between included and excluded patients are depicted in e-Table 2.

160

161 Clinical characteristics

162 The included patients had a mean age of 65 ± 8 years, 52% were male, 63% of the patients 163 experienced ≥ 2 exacerbations <12 months and 44% experienced ≥ 1 hospitalization <12 months.

164	Furthermore, 87% was highly symptomatic (mMRC \geq 2), and 45% of patients were
165	multimorbid. A 6MWT distance <350 meters was found in 38% of patient and the median
166	time-to-exhaustion on the CWRT was 230 (165-334) seconds. The isokinetic quadriceps peak
167	torque was 61±19% of predicted and the total work was 1487±632 J. Furthermore, 30% and
168	31% of the patients with COPD had a score ≥ 10 points on symptoms for anxiety and depression,
169	respectively. All details can be found in Tables 1 and 2.
170	
171	***** Tables 1 and 2 near here *****
172	
173	Short Physical Performance Battery
174	The SPPB summary score of the whole group was 9 (8-10) points. Ninety-eight patients (11%)
175	had LP scores, 393 patients (44%) had MP scores, and 409 patients (45%) had HP scores. The
176	frequency distribution of the SPPB summary score can be found in e-Figure 1.
177	The balance standing test score differed significantly among the levels of performance, with
178	the LP group performing the worst (p<0.001). Furthermore, the LP group executed the 4MGS
179	and 5STS (after excluding patients (n=70; whereof n=54 in LP group) who were not able to
180	perform the 5STS test), the slowest in comparison to the MP group and the HP group ($p<0.001$,
181	Table 3). The frequency distribution of the SPPB components can be found in Figure 1.
182	
183	***** Figure 1 and Table 3 near here ****
184	
185	Characteristics after stratification for SPPB
186	According to stratification for SPPB score, patients with LP scores were older, experienced
187	more dyspnoea, had a lower health status, had a higher percentage of ≥ 2 exacerbations and ≥ 1
188	hospitalizations in the past 12 months and were more likely long-term oxygen therapy users

than the MP and HP groups. Furthermore, 89% of the LP group and 79% of the MP group scored \geq 18 points on the CAT which was higher than the HP (68%) group (p<0.001, Table 1). The LP group had a higher GOLD classification and lower FEV₁ % predicted than MP and HP. The LP group showed lower arterial oxygen pressures and higher carbon dioxide pressures than the MP and HP group. The FFM of arms was lower (p=0.003) in the LP group in comparison to the HP group. The proportion of patients with a normal bone mineral density, osteopenia and osteoporosis was comparable between groups (Table 2).

Physical capacity was lowest in the LP group and highest in the HP group (all values p<0.001).
In the LP group had 96% of the patients a 6MWT distance <350 meters³⁴. This proportion was
lower in the MP group (46%) and HP group (16%). Furthermore, the LP group had on average
a lower CWRT time-to-exhaustion than the MP and HP group.

The muscle strength and endurance differed among the groups, with the LP group performing the worst, even after correcting for FFM (all values p<0.001, Table 2). Additionally, the LP group scored higher on symptoms of anxiety and depression and had a higher proportion of patients scoring ≥ 10 points on anxiety (46%) and depression (52%) in comparison to the MP and/or HP groups (all values, p<0.001, Table 2).

Even though, the HP group scored better on physical capacity and emotional status, still 8% of patients needed ≥ 1 stop during the 6MWT, the median Wmax on the maximal incremental cycle test was 54 (40-71)% of the predicted value and one-fourth of the patients had symptoms of anxiety and/or depression (Table 2).

209

210 Determinants of SPPB summary score

Almost all absolute phenotypic characteristics were univariate predictors of SPPB summary score (e-Table 3). Explanatory predictors without a high correlation with another variable of interest were entered in a multivariate linear regression model. This model (F(15,508)=13.673, p<0.001) explained 29% of the variance in SPPB summary score. Age (B=-0.085, p=0.043)
and 6MWT (meters) (B=0.454, p<0.001) were the only significant independent predictors (e-
Table 4).

217

218 **DISCUSSION**

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The present study shows that the phenotypic characteristics differ between patients with COPD after stratification for SPPB summary scores, with the worst values reported in the LP group. Moreover, patients with a SPPB summary score ≥ 10 points (HP group) can still exhibit impairments in physical capacity and emotional traits. Age and 6MWT (meters) were the only independent predictors in a multivariate regression model, explaining only 29% of the variance of SPPB summary score.

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In this study, 55% of the COPD patients scored <10 points on the SPPB at the pre-PR assessment, indicating a reduced functional capacity and increased risk of developing mobility and/or activities of daily living^{11,39}.

The LP group performed worse on all SPPB subtests in comparison to the MP and HP group. Furthermore, a lower quadriceps strength and 6MWT is reported in the LP group, this may, at least partly, explain the reduced SPPB performance. Recently, associations between the isometric quadriceps muscle strength, 6MWT, SPPB summary score and SPPB subtests scores have been reported which confirms our results^{15,16,40}.

Patients performed the 5STS worst of all SPPB subtests, which is consistent with the study of Larsson *et al.*⁴¹. Bernabeau-Mora *et al.* reported only an association between CAT and the 5STS (partial R^2 =0.073, p<0.001) in the multivariable regression model, and not with the other subtests. This supports the concept that the 5STS is a better screening tool for poor health status⁴⁰ than the other SPPB subtests. One possible reason is that ventilatory demands during
 5STS are higher than during the standing balance tests and 4MGS^{41,42} and is therefore more
 sensitive in obtaining differences between the performance group.

242

Overall, the phenotypic characteristics are worse in the LP group in comparison to the MP and
HP group. The reduced lung function in the LP group is in accordance with other studies as an
impaired lung function is known to contribute to mobility and balance deficits¹³. Furthermore,
Eisner *et al.* suggested that lung functional impairment may contribute to muscle weakness in
the upper and lower extremity of COPD patients, which is consistent with systemic involvement
from the disease⁴³.

The body composition, physical capacity and quadriceps muscle strength and endurance were 249 worse in the LP group, which is consistent with the studies of Patel et al. and Mohan et al.^{15,16}. 250 251 They reported lower quadriceps strength and bulk, physical activity, exercise capacity and performance in the LP and/or MP group in comparison to the HP group¹⁵ and decreased odds 252 of being in a lower category for the SPPB summary score for a longer 6MWT and greater 253 quadriceps maximal voluntary contraction strength¹⁶. Additionally, a decrease in FFM is 254 correlated with a decline in postural stability and mobility^{44,45}. A possible explanation can be 255 that a reduction in muscle mass is related to a loss in muscle function and strength⁴⁶, which are 256 both necessary to maintain balance and mobility and execute functional activities^{7,47-49}. 257

The emotional status differed between the three performance groups with the highest prevalence of anxiety and depression symptoms present in the LP group. The difference in anxiety between LP group and MP and HP group and in depression between LP and HP group reaches the minimal important difference⁵⁰. Other studies have already reported associations between anxiety, depression and mobility and balance which might explain the higher prevalence of symptoms of anxiety and depression in the LP group^{19,20,51}. A suggestion could be the increased risk of falls due to the inattention to potential environmental hazards in people with depression⁵²
or due to greater fear of falls in patients exhibiting anxiety or depression⁹. Contradictory,
physical activity is known to improve one's self-esteem and reduce depressive and anxiety
symptoms and less active patients may therefore develop more often emotional impairment⁵³.
Future studies are needed to determine the exact causal relationship and evaluate emotional
status more extensively.

270 Even though the values for phenotypic characteristics were the highest in the HP group, still 16% of the patients had a 6MWT distance <350 meters, which is a risk factor for respiratory 271 related hospitalization³⁴. Additionally, one out of four HP patients experienced symptoms of 272 273 anxiety and/or depression. These results indicate that even the HP patients with COPD at the start of PR can exhibit impairments in physical capacity and emotional status which cannot be 274 determined by the SPPB alone. This emphasizes the importance of additional assessment in 275 276 patients with COPD during baseline assessment in PR as SPPB alone cannot identify all patients at risk and/or in need for PR. 277

278

279 Many phenotypic factors were univariate predictors of the SPPB summary score, but age and 280 6MWT were the only independent predictors in a multivariate regression model. This finding 281 is consistent with the literature^{15,16,40} and highlights the importance of age and physical capacity 282 in maintaining balance and mobility.

283

284 Methodological considerations

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The strengths of the study are the large sample size of COPD patients with well-defined and well-characterized data which provides for the first time an extensive overview on phenotypic characteristics per SPPB performance of patients with COPD in a non-UK PR setting. The study confirms the high prevalence of physical and emotional impairment among all performancegroups.

Obviously, the cross-sectional design prevents us from establishing causality between patients' phenotypic factors and mobility and balance. Secondly, the data is obtained retrospectively from one location, which reduces the generalizability of the results. Current studies also need corroboration in the primary care setting.

295

296 CONCLUSIONS

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In COPD, patients with a LP SPPB summary score have the worst physical and emotional functioning. However, HP patients can still exhibit physical and emotional impairments. As the explained variance in SPPB summary score is low, the SPPB should not be considered as a screening tool to discriminate between COPD patients with a low or preserved physical capacity and emotional status.

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443 SUF	PPLIERS
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444	
445	A. MasterScreen PFT/ Body; Jaeger, Würzburg, Germany
446	B. Lunar iDXA; DEXAtech Benelux BV, Ridderkerk, the Netherlands
447	C. Ergoselect; Ergoline, Bitz, Germany
448	D. Technogym, Cesena, Italy
449	E. Biodex Multi-joint System 3; Biometrics Motion B.V., Groningen, the Netherlands
450	F. IBM North America, 590 Madison Ave, New York, NY 10022.
451	
452	
453	LEGENDS OF FIGURES
454	
455	Figure 1. Percentages (%) of patients of low-, moderate-, and high-performance group that
456	scored 0 to 4 on the (a) standing balance tests, (b) four meter gait speed (4MGS), and (c) five
457	sit-to-stand test (5STS).
458	e-Figure 1. The distribution (%) of the SPPB summary score within patients with COPD
459	starting pulmonary rehabilitation.

		Short Physical Performance Battery levels					
		Low-	Moderate-	High-	-		
Baseline characteristics	Patients with	Performance	Performance	Performance	p-value		
	(n=98) (n=		(n=393)	(n=393) (n=409)			
		General Character	istics				
Age (years)	65 ± 8	69 ± 8	66 ± 8	64 ± 8	<0.001 *,#,†		
Gender (male, %)	52	44	52	53	0.240		
Weight ^a (kg)	74 ± 20	76 ± 25	74 ± 19	73 ± 19	0.604		
BMI ^a (kg/m ²)	26.2 ± 6.3	27.3 ± 7.8	26.3 ± 6.1	25.7 ± 5.9	0.055		
mMRC ^b (grade)	2 (2-3)	4 (3-4)	3 (2-3)	2 (2-3)	<0.001 *,#,†		
mMRC \geq 2 ^b (% patients)	87	100	92	79	<0.001 *,#,†		
CAT ^c (points)	21 ± 7	25 ± 6	22 ± 6	20 ± 7	<0.001 *,#,†		
CAT \geq 10 ° (% patients)	95	100	96	93	0.009		
CAT \geq 18 ° (% patients)	75	89	79	68	<0.001 #,†		
Exacerbations in the past 12	20/17/20/14/8/21	6/17/10/22/5/20	22/16/10/14/0/20	22/19/24/11/9/16	<0.001 *.#		
months ^d : 0/1/2/3/4/>4	20/17/20/14/8/21	0/17/10/23/3/39	22/10/19/14/9/20	23/16/24/11/6/10	<0.001		
\geq 2 exacerbations in the past	63	77	63	50	0.006 *,#		
12 months ^d (% patients)	03 //		05	57	0.000 ,"		
Hospitalizations in the past	55/25/9/5/2/4	36/26/12/12/4/10	55/26/10/4/1/4	61/23/6/5/3/2	<0.001 *,#		
12 months ^e : 0/1/2/3/4/>4	5512519151214	30/20/12/12/ 1 /10	55/20/10/4/1/4	01/25/0/5/5/2	<0.001 "		
\geq 1 hospitalization in the							
past 12 months ^e (%	44	64	45	39	<0.001 *,#		
patients)							
CCI (points)	1 (1-2)	2 (1-3)	1 (1-2)	1 (1-2)	0.012		
$CCI \ge 2$ (% patients)	45	55	46	41	0.028		
Long-term O ₂ use ^f (yes, %	22	42	22	16	<0.001 *,#		
patients)	22	74	22	10	NU.001		

Table 1. Characteristics of patients with COPD stratified for SPPB summary score.

Data is presented as mean ± SD, median (IQR), or percentages. * indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 7-9. # indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 10-12. † indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 7-9 and SPPB 10-12. ‡ indicates no significant difference after Bonferroni post-hoc testing. Alphabetic characters in superscript indicates a sample size deviant from n = 900 with the following: a. n=897 (low, moderate, and high resp. 98, 393, 408), c. n=844 (low, moderate, and high resp. 87, 374, 383), d. n=895 (low, moderate, and high resp. 98, 390, 407), e. n=897 (low, moderate, and high resp. 96, 392, 409), f. n=883 (low, moderate, and high resp. 95, 387, 401). Abbreviations: BMI: Body Mass Index, CAT: COPD Assessment Test, COPD: chronic obstructive pulmonary disease, CCI: Charlson Comorbidity Index, kg: kilogram, m: meters, mMRC: Modified Medical Research Council, n: numbers, O2: oxygen, SPPB: Short Physical Performance Battery.

	Short Physical Performance Battery					
	Dation4a mith	Low-	Moderate-	High-	-	
Phenotypic characteristics		Performance	Performance	Performance	p-value	
	COPD (n=900)	(n=98)	(n=393)	(n=409)		
	Lung f	unction and arterial	blood gasses			
GOLD I/II/III/IV (%	0/20/22/24	2/20/21/28	11/07/20/02	10/20/20/20	0.007.*#	
patients)	9/29/38/24	2/30/31/38	11/2//39/23	10/30/39/22	0.007 ,#	
GOLD A/B/C/D ^a (%	5/24/8/62	0/15/0/95	2/27/5/66	0/04/12/54	-0 001 *#†	
patients)	5/24/8/05	0/15/0/85	3/2//5/00	9/24/13/34	<0.001 ,","	
FEV ₁ (% predicted)	43 (31-62)	35 (24-54)	43 (31-62)	44 (32-63)	0.001 *,#	
$FEV_{1}(L)$	1.07 (0.76-1.54)	0.81 (0.53-1.22)	1.05 (0.73-1.58)	1.13 (0.84-1.59)	<0.001 *,#	
FEV ₁ /FVC	0.35 (0.28-0.47)	0.34 (0.25-0.46)	0.36 (0.28-0.49)	0.35 (0.27-0.47)	0.283	
TLco SB ^b (% predicted)	50.1 ± 17.1	42.7 ± 16.3	49.7 ± 17.4	51.9 ± 16.6	<0.001 *,#	
RV-BB ^c (% predicted)	165.5 ± 55.7	181.0 ± 72.2	161.4 ± 56.5	166.0 ± 49.8	0.012	
TLC-BB ^d (% predicted)	117.3 ± 19.7	116.5 ± 24.7	115.3 ± 19.9	119.6 ± 17.9	0.013	
paO2 ^e (kPa)	9.1 (8.3-10)	8.6 (7.7-9.8)	9.0 (8.2-10.1)	9.3 (8.4-10.1)	0.001 *,#	
paCO2 ^f (kPa)	5.3 (4.9-5.9)	5.8 (5.1-6.8)	5.3 (4.9-5.9)	5.2 (4.9-5.7)	<0.001 *,#	
Saturation ^g (%)	94 (92-95)	92 (90-95)	93 (92-95)	94 (93-95)	0.181	
		Body composition	on			
FFMI ^h (kg/m ²)	16.6 ± 2.5	16.3 ± 2.8	16.6 ± 2.6	16.7 ±2.4	0.444	
FFM of the arms ^j (kg)	5.1 (3.9-6.5)	4.5 (3.6-6.0)	5.1 (3.9-6.3)	5.2 (4.2-6.7)	0.003 #	
FFM of the legs k (kg)	15.1 (12.2-17.9)	14.0 (11.7-17.0)	15.0 (12.1-17.8)	15.4 (12.5-18.0)	0.020	
Waist circumference ¹ (cm)	97.8 ± 17.1	101.3 ± 20.2	98.6 ± 16.9	96.2 ± 16.4	0.015	
Waist circumference above	74	76	76	70	0.276	
predicted values 1 (% patients)	74	70	70	12	0.276	
T-score L2L4 ^m	$\textbf{-0.79} \pm 1.72$	-0.60 ± 1.90	-0.80 ± 1.69	-0.83 ± 1.70	0.495	
T-score trochanter ⁿ	-1.76 ± 1.02	-1.95 ± 0.95	-1.81 ± 1.02	-1.66 ± 1.03	0.018	
Normal bone mineral density/						
osteopenia/ osteoporosis º (%	20/47/32	17/45/38	19/47/34	22/49/29	0.467	
patients)						
		Physical capacit	t y			
6MWT ^p (m)	389 (300-459)	194 (139-259)	360 (288-421)	441 (381-492)	<0.001 *,#,†	
6MWT < 350 m ^p (% patients)	38	96	46	16	<0.001 *,#,†	
6MWT ^q (% predicted)	62 (50-72)	33 (24-46)	58 (49-67)	69 (59-78)	<0.001 *,#,†	
6MWT: Patients with ≥ 1 stop	16	52	16	8	<0.001 *,#,†	
r (% patients)	10	32	10	0	\U.UU1	
Wmax ^s (W)	59 (43-80)	36 (23-53)	56 (41-76)	66 (49-90)	<0.001 *,#,†	
Wmax t (% of predicted)	49 (35-67)	31 (17-63)	46 (34-62)	54 (40-71)	<0.001 *,#,†	
CWRT TTE ^u (s)	230 (165-334)	145 (111-260)	213 (160-310)	254 (187-355)	<0.001 *,#,†	

Table 2. Phenotypic characteristics of patients with COPD stratified for SPPB summary scores.

Table 2 (continued).

Short Physical Performance Battery							
	Patients with	Low-	Moderate-	High-	-		
Physical status	COPD (n=900)	performance	performance	performance	p-value		
		(n=98)	(n=393)	(n=409)			
Isotonic muscle strength (1-RM)							
Leg press ^v (kg)	70 (50-100)	40 (20-60)	60 (40-90)	80 (60-110)	<0.001 *,#,†		
Leg extension ^w (kg)	28 (20-38)	18 (10-25)	25 (20-35)	30 (25-40)	<0.001 *,#,†		
Upper back x (kg)	23 (15-35)	15 (10-20)	20 (15-30)	25 (20-35)	<0.001 *,#,†		
Chest press ^y (kg)	23 (15-33)	18 (10-23)	20 (15-30)	25 (18-35)	<0.001 *,#,†		
	Isotonic mus	scle strength corre	cted for FFM				
Leg press ^z	4.83 ± 2.26	3.16 ± 1.98	4.40 ± 2.05	5.56 ± 2.20	<0.001 *,#,†		
Leg extension ^{za}	1.91 ± 0.70	1.36 ± 0.59	1.76 ± 0.66	2.15 ± 0.65	<0.001 *,#,†		
Upper back ^{zb}	4.67 ± 1.68	3.37 ± 1.60	4.47 ± 1.65	5.13 ± 1.56	<0.001 *,#,†		
Chest press ^{zc}	4.63 ± 1.68	3.58 ± 1.43	4.41 ± 1.69	5.04 ± 1.59	<0.001 *,#,†		
	Isokinetic mus	cle strength/endur	ance (BIODEX)				
Peak torque zd (Nm)	86 ± 33	60 ± 31	83 ± 33	93 ± 30	<0.001 *,#,†		
Peak torque ^{ze} (% predicted)	61 ± 19	46 ± 18	59 ± 19	65 ± 17	<0.001 *,#,†		
Total work ^{zd} (J)	1487 ± 632	889 ± 550	1400 ± 635	1648 ± 571	<0.001 *,#,†		
	Isokinetic muscle s	trength/endurance	e corrected for FFN	М			
Peak torque ^{zf} (Nm/kg)	5.57 ± 1.40	4.01 ± 1.45	5.36 ± 1.37	5.97 ± 1.21	<0.001 *,#,†		
Peak torque ^{zg} (%/kg)	4.06 ± 1.17	3.22 ± 1.23	3.94 ± 1.18	4.28 ± 1.08	<0.001 *,#,†		
Total work ^{zf} (J/kg)	95.5 ± 29.8	60.1 ± 29.5	89.8 ± 29.5	105.4 ± 24.4	<0.001 *,#,†		
		Emotional status	:				
HADS anxiety ^{zh} (points)	7.5 ± 4.2	9.2 ± 4.6	7.7 ± 4.1	6.9 ± 4.1	<0.001 *		
HADS anxiety $\geq 10^{\text{zh}}$ (%)	30	16	32	24	<0.001 #		
patients)		70	22	27	\0.001		
HADS depression ^{zh} (points)	7.4 ± 4.0	9.0 ± 4.4	7.8 ± 3.8	6.7 ± 4.0	<0.001 *,#,†		
HADS depression $\geq 10^{\text{zh}}$ (%)	31	52	31	25	<0.001 #,†		
patients)	51	52	51	25	\U.UU1		

Data is presented as mean \pm SD, median (IQR), or percentages. * indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 7-9. # indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 10-12. † indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 7-9 and SPPB 10-12. Alphabetic characters in superscript indicates a sample size deviant from n = 900 with the following: a. n=892 (low, moderate, and high resp. 96, 390, 406), b. n=835 (low, moderate, and high resp. 72, 363, 400), c. n=864 (low, moderate, and high resp. 90, 370, 404), d. n=865 (low, moderate, and high resp. 90, 371, 404), e. n=843 (low, moderate, and high resp. 81, 370, 392), f. n=843 (low, moderate, and high resp. 82, 370, 391), g. n=124 (low, moderate, and high resp. 13, 57, 54), h. n=891 (low, moderate, and high resp. 95, 389, 407), i. n=889 (low, moderate, and high resp. 96, 393, 408), m. n=881 (low, moderate, and high resp. 94, 384, 403), 96, 389, 407), l. n=897 (low, moderate, and high resp. 96, 393, 408), m. n=881 (low, moderate, and high resp. 94, 384, 403),

n. n=875 (low, moderate, and high resp. 91, 381, 403), o. n=888 (low, moderate, and high resp. 94, 388, 406), p. n=893 (low, moderate, and high resp. 95, 390, 408), q. n=893 (low, moderate, and high resp. 94, 390, 409), r. n=895 (low, moderate, and high resp. 95, 391, 409), s. n=822 (low, moderate, and high resp. 64, 359, 399), t. n=819 (low, moderate, and high resp. 64, 356, 399), u. n=796 (low, moderate, and high resp. 57, 347, 392), v. n=865 (low, moderate, and high resp. 87, 373, 405), w. n=834 (low, moderate, and high resp. 79, 366, 389), x. n=801 (low, moderate, and high resp. 80, 343, 378), y. n=794 (low, moderate, and high resp. 77, 342, 375), z. n=858 (low, moderate, and high resp. 85, 370, 403), za. n=828 (low, moderate, and high resp. 78, 363, 387), zb. n=796 (low, moderate, and high resp. 79, 341, 376), zc. n=789 (low, moderate, and high resp. 76, 340, 373), zd. n=690 (low, moderate, and high resp. 53, 285, 352), ze. n=689 (low, moderate, and high resp. 53, 285, 351), zf. n=684 (low, moderate, and high resp. 53, 281, 350), zg. n=683 (low, moderate, and high resp. 53, 281, 349). zh. n=843 (low, moderate, and high resp. 87, 374, 382). Abbreviations: BB: Body Box, COPD: chronic obstructive pulmonary disease, CWRT: Constant Work Rate Test, FEV1: Forced Expiratory Volume in the first second, FFM: Fat Free Mass, FFMI: Fat Free Mass index, FVC: Forced Vital Capacity, GOLD: Global Initiative for Chronic Obstructive Lung Disease, HADS: Hospital Anxiety and Depression Scale, J: Joule, kg: kilogram, L: liters, L2-L4: Lumbar spine (L2-L4), m: meters, Nm: Newton-meter, paCO2: Partial pressure of arterial carbon dioxide, paO₂: Partial pressure of arterial oxygen, SPPB: Short Physical Performance Battery, SB: single-breath, RV: Residual Volume, TLC: Total Lung Capacity, TLco: Diffusion capacity for carbon monoxide, TTE: time-to-exhaustion, Wmax: maximal wattage, W: wattage, 1-RM: One-Repetition Maximum, 6MWT: Six-Minute Walk Test..

Table 3. Short Physical Performance Battery (SPPB) results of patients with COPD stratified for SPPB summary scores.

		Short Phys				
CDDD acono	Dotionta with	Low-	Moderate-	High-		
SFFD score	COPD (= 000)	Performance	Performance	Performance	p-value	
	COPD (II=900)	(n=98)	(n=393)	(n=409)		
Balance side-by-side	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	-0.001 *#	
(s)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	<0.001 "	
Balance semi-	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	10.0 (10.0, 10.0)	<0.001 *.#	
tandem (s)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	10.0 (10.0-10.0)	<0.001	
Balance tandem (s)	10.0 (10.0-10.0)	0.0 (0.0-5.5)	10.0 (7.3-10.0)	10.0 (10.0-10.0)	<0.001 *,#,†	
4MGS (s)	3.8 (3.2-4.7)	6.3 (4.9-7.9)	4.2 (3.6-5.0)	3.4 (3.0-3.9)	<0.001 *,#,†	
4MGS ^a (m/s)	1.04 ± 0.28	0.62 ± 0.20	0.98 ± 0.24	1.19 ± 0.23	<0.001 *,#,†	
5STS (s) – all	15.0 (12.3, 18.4)	0 (0 0 22 0)	18.2 (16.0.21.4)	131(116147)	<0.001 *.7	
patients	13.0 (12.3-18.4)	0 (0.0-22.0)	18.2 (10.0-21.4)	13.1 (11.0-14.7)	<0.001 ''	
5STS ^b (s) – only						
patients able to	15.4 (12.9-18.8)	23.3 (19.3-31.4)	18.4 (16.6-21.6)	13.1 (11.6-14.7)	<0.001 *,#,†	
perform the test						
Total SPPB score	9 (8-10)	5 (1-6)	$0(8_{-}0)$	11 (10-11)	<0.001 *,#,†	
(points)	9 (8-10)	5 (4-0)) (0-9)	11 (10-11)	<0.001 ,"","	

Data is presented as mean \pm SD or median (IQR). * indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 7-9. # indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 0-6 and SPPB scores 10-12. † indicates a significant difference after Bonferroni post-hoc correction between SPPB scores 7-9 and SPPB 10-12. Alphabetic characters in superscript indicates a sample size deviant from n = 900 with the following: a. n=884 (low, moderate, and high resp. 82, 393, 409), b. n=830 (low, moderate, and high resp. 44, 377, 409). Abbreviations: COPD: Chronic Obstructive Pulmonary Disease, m: meters, s: seconds, SPPB: Short Physical Performance Battery, 4MGS: Four-Meter Gait Speed, 5STS: Five Sit-To-Stand. Supplemental Table S2. Differences in patients' characteristics between included and excluded

patients.

Age (y), mean \pm SD	65±8	63±12	.140				
Sex (male, % of patients)	52	55	.397				
Weight (kg), mean ± SD ^a	74±20	75±16	.728				
BMI (kg/m ²), mean \pm SD ^a	26.2±6.3	26.4±5.7	.806				
mMRC (grade), median (IQR) b	2 (2-3)	3 (2-4)	<.001				
CAT (points), mean ± SD °	21±7	23±6	.047				
Exacerbations in the past 12 mo: 0/1/2/3/4/>4 (% of patients) ^d	20/17/20/14/8/21	11/10/17/13/6/43	.006				
Hospitalizations in the past 12 mo: 0/1/2/3/4/>4 (% of patients) ^e	55/25/9/5/2/4	39/26/13/20/2/0	.001				
CCI (points), median (IQR)	1 (1-2)	1 (1-2)	.600				
Long-term O2 use (yes, % patients) ^f	22	37	.015				
Lung function and arte	rial blood gases						
FEV ₁ (L), median (IQR) ^g	1.07 (0.76-1.54)	0.86 (0.69-1.47)	.070				
paO2 (kPa), median (IQR) ^h	9.1 (8.3-10.0)	9.3 (8.1-11.1)	.270				
paCO ₂ (kPa), median (IQR) ⁱ	5.3 (4.9-5.9)	5.2 (4.8-5.7)	.180				
Saturation (%), median (IQR) ^h	94 (92-95)	94 (91-97)	.247				
Body compos	sition						
FFM of the arms (kg), median (IQR) ^j	5.1 (3.9-6.5)	4.6 (3.8-6.0)	.081				
FFM of the legs (kg), median (IQR) ^j	15.1 (12.2-17.9)	14.3 (11.3-16.8)	.061				
Waist circumference (cm), mean ± SD ^k	97.8±17.1	96.1±14.9	.504				
T score lumbar spine (L2-L4), mean \pm SD ¹	-0.79±1.72	-1.11±1.56	.198				
T score hip (trochanter), mean \pm SD ^m	-1.76±1.02	-1.85±1.15	.522				
Physical capacity and ex	xercise tolerance						
6MWT (m), median (IQR) ⁿ	389 (300-459)	351 (259-428)	.049				
Wmax (W), median (IQR) ^o	59 (43-80)	56 (42-80)	.694				
CWRT TTE (s), median (IQR) ^p	230 (165-334)	184 (151-237)	.044				
Isotonic muscle	strength						
Leg press (kg), median (IQR) ^q	70 (50-100)	50 (30-90)	.027				
Leg extension (kg), median (IQR) ^r	28 (20-38)	20 (15-39)	.053				
Upper back (kg), median (IQR) ^s	23 (15-35)	30 (15-35)	.509				
Chest press (kg), median (IQR) ^t	23 (15-33)	25 (13-30)	.428				
Isokinetic muscle strength/endurance							
Peak torque (Nm), mean ± SD ^u	86±33	75±28	.041				
Total work (J), mean ± SD ^u	1487±632	1197±529	.009				
Emotional status							
HADS anxiety (points), mean \pm SD ^v	7.5±4.2	8.5±4.5	.106				
HADS depression (points), mean \pm SD v	7.4±4.0	7.4±3.9	.952				
Short Physical Perform	nance Battery						

Balance tests score, median (IQR)	4 (4-4)	4 (3-4)	.300
4MGS score, median (IQR)	4 (4-4)	4 (3-4)	.001
5STS score, median (IQR) w	2 (1-3)	1 (1-3)	.010
SPPB total score, median (IQR) w	9 (8-10)	8 (7-11)	.009

Alphabetic characteristics in superscript indicates a sample size deviant from n = 953 with the following: a = 927 (included = 897 and excluded = 31), b = 952 (included = 899 and excluded = 53), c = 894 (included = 844 and excluded = 50), d = 948 (included = 895 and excluded = 53), e = 910 (included = 864 and excluded = 46), f = 935 (included = 884 and excluded 51), g = 951 (included = 899 and excluded = 52), h = 881 (included = 840 and excluded = 41), i = 882 (included = 841 and excluded = 41), j = 935 (included = 885 and excluded = 50), k = 949 (included 891 and excluded = 50), l = 923 (included = 874 and excluded = 49), m = 916 (included = 868 and excluded = 48), n = 916 (included = 875 and excluded = 41), o = 832 (included = 796 and excluded = 36), p = 858 (included = 822 and excluded = 36), q = 909 (included = 865 and excluded = 44), r = 878 (included = 834 and excluded = 44), s = 825 (included = 801 and excluded = 24), t = 830 (included = 794 and excluded = 36), u = 720 (included = 687 and excluded = 33), v = 892 (included = 843 and excluded = 49), w = 952 (included = 900 and excluded 52). Abbreviations: BMI, Body Mass Index; CAT, COPD Assessment Test; CCI, Charlson Comorbidity Index; CWRT, Constant Work Rate Test; FEV1, Forced Expiratory Volume in the first second; FFM, Fat-Free Mass; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; mMRC, Modified Medical Research Council; paCO2, Partial Pressure of arterial carbon dioxide; paO2, Partial pressure of arterial oxygen; O2, oxygen; SD, standard deviation; SPPB, Short Physical Performance Battery; TTE, time-to-exhaustion; Wmax, maximal workload; 4MGS, 4-M Gait Speed; 5STS, 5-repetition Sit-To-Stand; 6MWT, 6-Minute Walk Test.

Supplemental Table S3. Univariate regression models of patients' characteristics and the SPPB summary score.

Patients' characteristics	Model	ANOVA		Coefficient		P Value	
	Adjusted R ²	F-value	Df	Beta	CI		
Age (y)	0.056	54.415	898	-0.060	-0.0760.044	<.001	
Sex (Female/Male)	0.001	2.017	898	-0.196	-0.468- 0.075	.156	
Weight (kg)	-0.001	0.459	895	-0.002	-0.009- 0.005	.498	
BMI (kg/m ²)	0.003	3.928	895	-0.022	-0.044- 0.000	.048	
mMRC (grade)	0.200	225.840	897	-0.920	-1.0400.799	<.001	
CAT (points)	0.058	52.603	843	-0.075	-0.0950.055	<.001	
Exacerbations in the past 12 months	0.031	29.277	893	-0.207	-0.2820.132	<.001	
Hospitalizations in the past 12 months	0.033	31.642	895	-0.300	-0.4040.195	<.001	
CCI (points)	0.011	11.262	898	-0.179	-0.2830.074	.001	
Long-term O ₂ use (yes/no)	0.042	39.922	881	1.047	0.722- 1.372	<.001	
Lung	function and a	arterial bloc	od gases	5			
$FEV_1(L)$	0.026	24.938	898	0.523	0.318-0.729	<.001	
paO ₂ (kPa)	0.012	11.482	841	0.160	0.067-0.253	.001	
paCO ₂ (kPa)	0.046	41.178	841	-0.498	-0.6510.346	<.001	
Saturation (%)	0.009	2.111	122	0.096	-0.035-0.226	.149	
Body composition							
FFM of the arms (kg)	0.012	11.815	890	0.142	0.061-0.223	.001	
FFM of the legs (kg)	0.009	9.524	890	0.053	0.019-0.087	.002	
Waist circumference (cm)	0.007	7.152	895	-0.011	-0.0190.003	.008	
T score lumbar spine (L2-L4)	0.000	0.643	879	-0.033	-0.112-0.047	.423	
T score hip (trochanter)	0.006	5.973	873	0.167	0.033-0.300	.015	
Physi	cal capacity an	d exercise t	oleranc	e			
6MWT (m)	0.422	653.200	891	0.012	0.011-0.013	<.001	
Wmax (W)	0.097	89.162	820	0.017	0.014-0.021	<.001	
CWRT TTE (s)	0.023	20.127	794	0.001	0.001-0.002	<.001	
	Isotonic mus	cle strength	ı				
Leg press (kg)	0.110	107.639	863	0.016	0.013-0.019	<.001	
Leg extension (kg)	0.114	107.754	832	0.048	0.039-0.057	<.001	
Upper back (kg)	0.075	66.264	799	0.041	0.031-0.051	<.001	
Chest press (kg)	0.061	52.926	792	0.038	0.028-0.048	<.001	
Isok	inetic muscle st	trength/end	urance				
Peak torque (Nm)	0.090	69.351	688	0.018	0.014-0.022	<.001	
Total work (J)	0.130	103.696	688	0.001	0.001-0.001	<.001	
Emotional status							
HADS anxiety (points)	0.026	23.885	841	-0.081	-0.1130.048	<.001	
HADS depression (points)	0.039	34.742	841	-0.102	-0.1360.068	<.001	

Abbreviations: BMI, Body Mass Index; CAT, COPD Assessment Test; CCI, Charlson Comorbidity Index; CI, Confidence Interval; CWRT, Constant Work Rate Test; DF, Degrees of Freedom; FEV₁, Forced Expiratory Volume in the first second; FFM, Fat Free Mass; HADS, Hospital Anxiety and Depression Scale; mMRC, Modified Medical Research Council; paCO₂, Partial Pressure of arterial carbon dioxide; paO₂, Partial pressure of arterial oxygen; O₂, oxygen; SPPB, Short Physical Performance Battery; TTE, time-to-exhaustion; Wmax, maximal workload; 6MWT, 6-Minute Walk Test. Supplemental Table S4. Multivariate regression model using the enter method to predict the SPPB

summary score.

Independent variable	Estimate	Standard error	B standardized	P Value	Partial R ²
Age (y)	-0.016	0.008	-0.085	.043	-0.090
mMRC (grade)	-0.023	0.075	-0.015	.757	-0.014
CAT (points)	-0.007	0.010	-0.029	.519	-0.029
Exacerbations in the past 12 months	0.039	0.039	0.045	.316	0.045
Hospitalizations in the past 12 months	-0.014	0.060	-0.010	.810	-0.011
CCI (points)	-0.061	0.049	-0.049	.212	-0.055
Long-term O ₂ use (yes/no)	-0.084	0.168	-0.020	.617	-0.022
paO ₂ (kPa)	-0.004	0.041	-0.004	.917	-0.005
paCO ₂ (kPa)	0.045	0.078	0.025	.563	0.026
Waist circumference (cm)	-0.006	0.004	-0.072	.141	-0.065
T score hip (trochanter)	-0.066	0.061	-0.045	.282	-0.048
6MWT (m)	0.007	0.001	0.454	<.001	0.342
CWRT TTE (s)	>0.001	0.000	-0.001	.979	-0.001
Total work (J)	0.000	0.000	0.056	.292	0.047
HADS depression (points)	-0.019	0.016	-0.048	.249	-0.051

Abbreviations: B, Beta; CAT, COPD Assessment Test; CCI, Charlson Comorbidity Index; CWRT, Constant Work Rate Test; HADS, Hospital Anxiety and Depression Scale; mMRC, Modified Medical Research Council; paCO₂, Partial Pressure of arterial carbon dioxide; paO₂, Partial pressure of arterial oxygen; O₂, oxygen; SPPB, Short Physical Performance Battery; TTE, time-to-exhaustion; 6MWT, 6-Minute Walk Test.









Supplemental Table S1. The scoring system of the standing balance, 4-m gait speed (4MGS) and 5-repetition sit-to-stand (5STS) tests.

	Balance: Side by side	Balance: semitandem	Balance: tandem	4MGS	5STS
Scores	Seconds	Seconds	Seconds	Seconds	Seconds
4				< 4.82	< 11.20
3				4.82 - 6.20	11.20 - 13.69
2			10.00	6.21 - 8.70	13.70 - 16.69
1	10.00	10.00	3.00-9.99	> 8.70	16.7 - 60
0	< 10.00	< 10.00	< 3.00	Not able to perform test	Not able to perform test