

Phenotypic Characteristics of Patients With Chronic Obstructive
Pulmonary Disease After Stratification for the Short Physical
Performance Battery Summary Score

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TITLE: Phenotypic characteristics of patients with Chronic Obstructive Pulmonary Disease after stratification for the Short Physical Performance Battery summary score.

RUNNING HEAD: Mobility and balance in COPD.

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1 **TITLE: Phenotypic characteristics of patients with Chronic Obstructive Pulmonary**
2 **Disease after stratification for the Short Physical Performance Battery summary score.**

3

4 **ABSTRACT**

5

6 **Objective:** To assess the phenotypic characteristics of patients with Chronic Obstructive
7 Pulmonary Disease (COPD) after stratification for Short Physical Performance Battery (SPPB)
8 summary scores and to determine phenotypic characteristics of the SPPB summary score at the
9 start of pulmonary rehabilitation (PR).

10 **Design:** Retrospective, cross-sectional.

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

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

14 **Interventions:** Not applicable.

15 **Main outcome measure:** Patients were stratified according to their SPPB summary scores into
16 low-performance (LP), moderate-performance (MP) or high-performance (HP). Furthermore,
17 lung function, arterial blood gases, body composition, physical capacity, lower-limb muscle
18 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

39

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

47 The Short Physical Performance Battery (SPPB) is a commonly used, simple and quick
48 performance measure to evaluate mobility and balance, and is recommended in older patients
49 by the European Medicines Agency¹³. Furthermore, the SPPB score has prognostic value as it
50 might identify a subsequent decline in activities of daily living status, rehospitalization and
51 mortality in elderly, including COPD, after hospital discharge¹⁴. Individuals can be grouped
52 based on their SPPB summary score into a low-performance (LP), a moderate-performance
53 (MP), and a high-performance (HP) group¹¹. Patel *et al.* and Mohan *et al.* were the first to
54 evaluate the physical phenotypic characteristics of the abovementioned SPPB performance
55 groups in patients with COPD^{15,16}. Indeed, LP patients with COPD had more functional
56 impairment, loss of muscle mass and structural muscle abnormality compared to HP patients¹⁵.
57 Furthermore, a longer 6-minute walk test (6MWT) distance, greater quadriceps maximal
58 voluntary contraction strength, lower age, self-reported hypertension and dyspnea, and being
59 married decreased the likelihood of being in the LP group¹⁶. These data need further
60 corroboration in a non-UK-based settings, as geographic differences in clinical characteristics
61 and management of COPD are known¹⁷.

62 Symptoms of anxiety and depression are also common in patients with COPD¹⁸, and
63 significantly correlate with mobility and balance in healthy elderly^{19,20}. However, it remains
64 unclear whether and to what extent a similar pattern occurs in emotional status (i.e. symptoms

65 of anxiety and depression) after stratification for SPPB summary scores. Furthermore, it is
66 unclear whether and to what extent physical and emotional impairment is also present in HP
67 patients. This is important to know, as HP patients may give a first impression that they have a
68 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**

74

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

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

88

89 **Baseline characteristics**

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

95

96 **Short Physical Performance Battery**

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

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

108

109 **Phenotypic characteristics**

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

114 Waist circumference was measured and fat-free mass (FFM) and T-scores of the hip
115 (trochanter) and lumbar spine (L2-L4) were evaluated using dual energy x-ray absorptiometry
116 (DEXA) (Lunar iDXA^b)²⁹. The FFM index was calculated by dividing FFM by height*height.
117 The reference values of International Diabetes Federation were used for waist circumference³⁰.
118 Physical capacity was assessed using the 6 minute walk test (6MWT), maximal incremental
119 cardiopulmonary exercise test and constant work rate test (CWRT). The 6MWT was performed
120 indoor, on a flat and straight walking course of 30 meters, following the ERS/ATS
121 guidelines^{31,32}. Reference values from Troosters *et al.*³³ were used and a cutoff value of 350
122 meters according to Spruit *et al.* was applied to predict respiratory related hospitalization³⁴. The
123 maximal cardiopulmonary exercise test was performed on an electromagnetically braked cycle
124 ergometer (Ergoselect^c) according to the recommended guidelines³⁵. The maximal workload
125 (Wmax) was calculated as a percentage of the predicted value³⁶. The CWRT was performed on
126 the same ergometer at 75% of the predetermined Wmax. Patients cycled until symptom
127 limitation or until pedaling rate decreased under 60 rpm (with a maximum of 20 minutes)³⁷.
128 Isotonic muscle strength was measured by one repetition-maximum leg press, leg extension,
129 upper back and chest press using standard weight training apparatus (Technogym^d) and was
130 corrected for the FFM of the legs or arms. Isokinetic quadriceps peak torque (Nm) and
131 endurance (total amount of delivered work, J) of the right leg were assessed with a computerized
132 dynamometer (Biodex Multi-joint System 3^e) and also corrected for the FFM of the legs.
133 Patients performed a set of 30 repetitions at an angular speed of 90°/s.
134 The Hospital Anxiety and Depression Scale was used as a screening tool to detect symptoms
135 of anxiety and depression. A cutoff point of >10 points was used for each domain³⁸.

136

137 **Statistical analyses**

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

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

153

154 **RESULTS**

155

156 Nine hundred of the 953 patients with COPD were analysed. Reasons for exclusion were
157 absence of SPPB data (n=1), being younger than 40 years (n=5), participating in the PR program
158 for the second time (n=20), and erroneous download from the database (n=27). Differences
159 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 ≥ 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 $61 \pm 19\%$ 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

189 than the MP and HP groups. Furthermore, 89% of the LP group and 79% of the MP group
190 scored ≥ 18 points on the CAT which was higher than the HP (68%) group ($p < 0.001$, Table 1).
191 The LP group had a higher GOLD classification and lower FEV₁ % predicted than MP and HP.
192 The LP group showed lower arterial oxygen pressures and higher carbon dioxide pressures than
193 the MP and HP group. The FFM of arms was lower ($p = 0.003$) in the LP group in comparison
194 to the HP group. The proportion of patients with a normal bone mineral density, osteopenia and
195 osteoporosis was comparable between groups (Table 2).
196 Physical capacity was lowest in the LP group and highest in the HP group (all values $p < 0.001$).
197 In the LP group had 96% of the patients a 6MWT distance < 350 meters³⁴. This proportion was
198 lower in the MP group (46%) and HP group (16%). Furthermore, the LP group had on average
199 a lower CWRT time-to-exhaustion than the MP and HP group.
200 The muscle strength and endurance differed among the groups, with the LP group performing
201 the worst, even after correcting for FFM (all values $p < 0.001$, Table 2). Additionally, the LP
202 group scored higher on symptoms of anxiety and depression and had a higher proportion of
203 patients scoring ≥ 10 points on anxiety (46%) and depression (52%) in comparison to the MP
204 and/or HP groups (all values, $p < 0.001$, Table 2).
205 Even though, the HP group scored better on physical capacity and emotional status, still 8% of
206 patients needed ≥ 1 stop during the 6MWT, the median Wmax on the maximal incremental cycle
207 test was 54 (40-71)% of the predicted value and one-fourth of the patients had symptoms of
208 anxiety and/or depression (Table 2).

209

210 **Determinants of SPPB summary score**

211 Almost all absolute phenotypic characteristics were univariate predictors of SPPB summary
212 score (e-Table 3). Explanatory predictors without a high correlation with another variable of
213 interest were entered in a multivariate linear regression model. This model ($F(15,508) = 13.673$,

214 p<0.001) explained 29% of the variance in SPPB summary score. Age (B=-0.085, p=0.043)
215 and 6MWT (meters) (B=0.454, p<0.001) were the only significant independent predictors (e-
216 Table 4).

217

218 **DISCUSSION**

219

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

226

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

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

235 Patients performed the 5STS worst of all SPPB subtests, which is consistent with the study of
236 Larsson *et al.*⁴¹. Bernabeu-Mora *et al.* reported only an association between CAT and the 5STS
237 (partial $R^2=0.073$, p<0.001) in the multivariable regression model, and not with the other
238 subtests. This supports the concept that the 5STS is a better screening tool for poor health

239 status⁴⁰ than the other SPPB subtests. One possible reason is that ventilatory demands during
240 5STS are higher than during the standing balance tests and 4MGS^{41,42} and is therefore more
241 sensitive in obtaining differences between the performance group.

242

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

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

258 The emotional status differed between the three performance groups with the highest prevalence
259 of anxiety and depression symptoms present in the LP group. The difference in anxiety between
260 LP group and MP and HP group and in depression between LP and HP group reaches the
261 minimal important difference⁵⁰. Other studies have already reported associations between
262 anxiety, depression and mobility and balance which might explain the higher prevalence of
263 symptoms of anxiety and depression in the LP group^{19,20,51}. A suggestion could be the increased

264 risk of falls due to the inattention to potential environmental hazards in people with depression⁵²
265 or due to greater fear of falls in patients exhibiting anxiety or depression⁹. Contradictory,
266 physical activity is known to improve one's self-esteem and reduce depressive and anxiety
267 symptoms and less active patients may therefore develop more often emotional impairment⁵³.
268 Future studies are needed to determine the exact causal relationship and evaluate emotional
269 status more extensively.

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

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**

285

286 The strengths of the study are the large sample size of COPD patients with well-defined and
287 well-characterized data which provides for the first time an extensive overview on phenotypic
288 characteristics per SPPB performance of patients with COPD in a non-UK PR setting. The study

289 confirms the high prevalence of physical and emotional impairment among all performance
290 groups.

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

295

296 **CONCLUSIONS**

297

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

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442

443 **SUPPLIERS**

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.

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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.

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

Baseline characteristics	Patients with COPD (n=900)	Short Physical Performance Battery levels			p-value
		Low-Performance (n=98)	Moderate-Performance (n=393)	High-Performance (n=409)	
General Characteristics					
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 ≥ 2 ^b (% patients)	87	100	92	79	<0.001 ^{*,†}
CAT ^c (points)	21 ± 7	25 ± 6	22 ± 6	20 ± 7	<0.001 ^{*,†}
CAT ≥ 10 ^c (% patients)	95	100	96	93	0.009
CAT ≥ 18 ^c (% patients)	75	89	79	68	<0.001 ^{*,†}
Exacerbations in the past 12 months ^d : 0/1/2/3/4/>4	20/17/20/14/8/21	6/17/10/23/5/39	22/16/19/14/9/20	23/18/24/11/8/16	<0.001 ^{*,#}
≥ 2 exacerbations in the past 12 months ^d (% patients)	63	77	63	59	0.006 ^{*,#}
Hospitalizations in the past 12 months ^e : 0/1/2/3/4/>4	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 ^{*,#}
≥ 1 hospitalization in the past 12 months ^e (% patients)	44	64	45	39	<0.001 ^{*,#}
CCI (points)	1 (1-2)	2 (1-3)	1 (1-2)	1 (1-2)	0.012
CCI ≥ 2 (% patients)	45	55	46	41	0.028
Long-term O ₂ use ^f (yes, % patients)	22	42	22	16	<0.001 ^{*,#}

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, 390, 409), b. n=899 (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.

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

Phenotypic characteristics	Patients with COPD (n=900)	Short Physical Performance Battery			p-value
		Low-Performance (n=98)	Moderate-Performance (n=393)	High-Performance (n=409)	
Lung function and arterial blood gasses					
GOLD I/II/III/IV (% patients)	9/29/38/24	2/30/31/38	11/27/39/23	10/30/39/22	0.007 ^{*,#}
GOLD A/B/C/D ^a (% patients)	5/24/8/63	0/15/0/85	3/27/5/66	9/24/13/54	<0.001 ^{*,#,†}
FEV₁ (% predicted)	43 (31-62)	35 (24-54)	43 (31-62)	44 (32-63)	0.001 ^{*,#}
FEV₁ (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 ^{*,#}
FEV₁/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
TL_{CO} 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					
FFMI ^h (kg/m²)	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 ^l (cm)	97.8 ± 17.1	101.3 ± 20.2	98.6 ± 16.9	96.2 ± 16.4	0.015
Waist circumference above predicted values ^l (% patients)	74	76	76	72	0.276
T-score L2L4 ^m	-0.79 ± 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 (% patients)	20/47/32	17/45/38	19/47/34	22/49/29	0.467
Physical capacity					
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 ^r (% patients)	16	52	16	8	<0.001 ^{*,#,†}
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 (continued).

Physical status	Patients with COPD (n=900)	Short Physical Performance Battery			p-value
		Low-performance (n=98)	Moderate-performance (n=393)	High-performance (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 ^{*,#,\dagger}
Leg extension ^w (kg)	28 (20-38)	18 (10-25)	25 (20-35)	30 (25-40)	<0.001 ^{*,#,\dagger}
Upper back ^x (kg)	23 (15-35)	15 (10-20)	20 (15-30)	25 (20-35)	<0.001 ^{*,#,\dagger}
Chest press ^y (kg)	23 (15-33)	18 (10-23)	20 (15-30)	25 (18-35)	<0.001 ^{*,#,\dagger}
Isotonic muscle strength corrected for FFM					
Leg press ^z	4.83 ± 2.26	3.16 ± 1.98	4.40 ± 2.05	5.56 ± 2.20	<0.001 ^{*,#,\dagger}
Leg extension ^{za}	1.91 ± 0.70	1.36 ± 0.59	1.76 ± 0.66	2.15 ± 0.65	<0.001 ^{*,#,\dagger}
Upper back ^{zb}	4.67 ± 1.68	3.37 ± 1.60	4.47 ± 1.65	5.13 ± 1.56	<0.001 ^{*,#,\dagger}
Chest press ^{zc}	4.63 ± 1.68	3.58 ± 1.43	4.41 ± 1.69	5.04 ± 1.59	<0.001 ^{*,#,\dagger}
Isokinetic muscle strength/endurance (BIODEX)					
Peak torque ^{zd} (Nm)	86 ± 33	60 ± 31	83 ± 33	93 ± 30	<0.001 ^{*,#,\dagger}
Peak torque ^{ze} (% predicted)	61 ± 19	46 ± 18	59 ± 19	65 ± 17	<0.001 ^{*,#,\dagger}
Total work ^{zd} (J)	1487 ± 632	889 ± 550	1400 ± 635	1648 ± 571	<0.001 ^{*,#,\dagger}
Isokinetic muscle strength/endurance corrected for FFM					
Peak torque ^{zf} (Nm/kg)	5.57 ± 1.40	4.01 ± 1.45	5.36 ± 1.37	5.97 ± 1.21	<0.001 ^{*,#,\dagger}
Peak torque ^{zg} (%/kg)	4.06 ± 1.17	3.22 ± 1.23	3.94 ± 1.18	4.28 ± 1.08	<0.001 ^{*,#,\dagger}
Total work ^{zf} (J/kg)	95.5 ± 29.8	60.1 ± 29.5	89.8 ± 29.5	105.4 ± 24.4	<0.001 ^{*,#,\dagger}
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 ≥ 10 ^{zh} (% patients)	30	46	32	24	<0.001 [#]
HADS depression ^{zh} (points)	7.4 ± 4.0	9.0 ± 4.4	7.8 ± 3.8	6.7 ± 4.0	<0.001 ^{*,#,\dagger}
HADS depression ≥ 10 ^{zh} (% patients)	31	52	31	25	<0.001 ^{*,#,\dagger}

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. 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. 95, 387, 407), j. n=892 (low, moderate, and high resp. 95, 390, 407), k. n=892 (low, moderate, and high resp. 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.

SPPB score	Patients with COPD (n=900)	Short Physical Performance Battery levels			p-value
		Low-Performance (n=98)	Moderate-Performance (n=393)	High-Performance (n=409)	
Balance side-by-side (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-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 patients	15.0 (12.3-18.4)	0 (0.0-22.0)	18.2 (16.0-21.4)	13.1 (11.6-14.7)	<0.001 ^{*,†}
5STS ^b (s) – only patients able to perform the test	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 ^{*,#,†}
Total SPPB score (points)	9 (8-10)	5 (4-6)	9 (8-9)	11 (10-11)	<0.001 ^{*,#,†}

Data is presented as mean ± 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.

Patients' characteristics	Included (n=900)	Excluded (n=53)	P Value
Age (y), mean \pm SD	65 \pm 8	63 \pm 12	.140
Sex (male, % of patients)	52	55	.397
Weight (kg), mean \pm SD ^a	74 \pm 20	75 \pm 16	.728
BMI (kg/m ²), mean \pm SD ^a	26.2 \pm 6.3	26.4 \pm 5.7	.806
mMRC (grade), median (IQR) ^b	2 (2-3)	3 (2-4)	<.001
CAT (points), mean \pm SD ^c	21 \pm 7	23 \pm 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 O ₂ use (yes, % patients) ^f	22	37	.015
Lung function and arterial blood gases			
FEV ₁ (L), median (IQR) ^g	1.07 (0.76-1.54)	0.86 (0.69-1.47)	.070
paO ₂ (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 composition			
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 \pm SD ^k	97.8 \pm 17.1	96.1 \pm 14.9	.504
T score lumbar spine (L2-L4), mean \pm SD ^l	-0.79 \pm 1.72	-1.11 \pm 1.56	.198
T score hip (trochanter), mean \pm SD ^m	-1.76 \pm 1.02	-1.85 \pm 1.15	.522
Physical capacity and exercise 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 \pm SD ^u	86 \pm 33	75 \pm 28	.041
Total work (J), mean \pm SD ^u	1487 \pm 632	1197 \pm 529	.009
Emotional status			
HADS anxiety (points), mean \pm SD ^v	7.5 \pm 4.2	8.5 \pm 4.5	.106
HADS depression (points), mean \pm SD ^v	7.4 \pm 4.0	7.4 \pm 3.9	.952
Short Physical Performance 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	-0.076- -0.044	<.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	-1.040- -0.799	<.001
CAT (points)	0.058	52.603	843	-0.075	-0.095- -0.055	<.001
Exacerbations in the past 12 months	0.031	29.277	893	-0.207	-0.282- -0.132	<.001
Hospitalizations in the past 12 months	0.033	31.642	895	-0.300	-0.404- -0.195	<.001
CCI (points)	0.011	11.262	898	-0.179	-0.283- -0.074	.001
Long-term O ₂ use (yes/no)	0.042	39.922	881	1.047	0.722- 1.372	<.001
Lung function and arterial blood gases						
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	-0.651- -0.346	<.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	-0.019- -0.003	.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
Physical capacity and exercise tolerance						
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 muscle strength						
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
Isokinetic muscle strength/endurance						
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	-0.113- -0.048	<.001
HADS depression (points)	0.039	34.742	841	-0.102	-0.136- -0.068	<.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; W_{max}, 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.

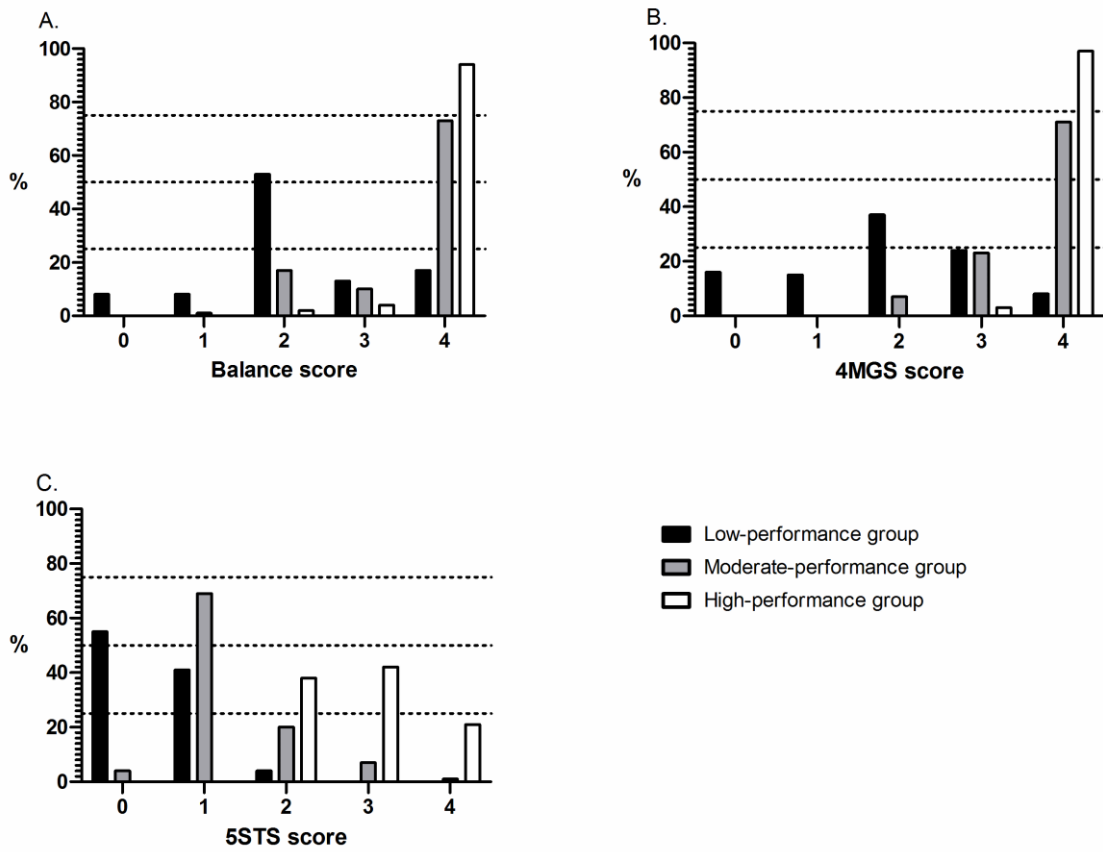
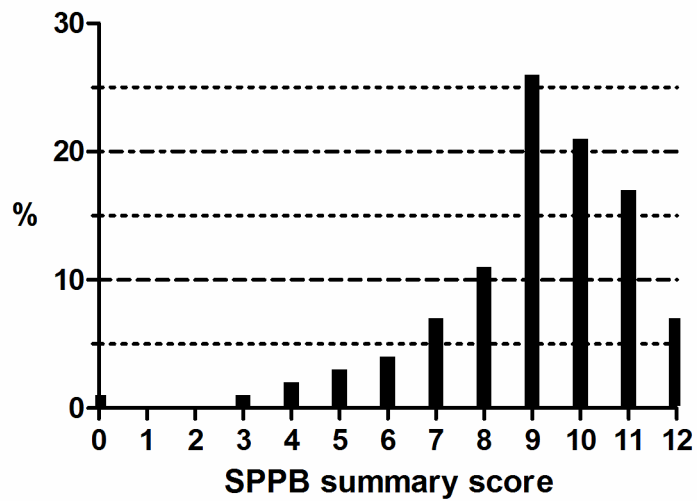


Figure 1



Supplemental fig S1

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