

1 **Functional balance in older adults with Chronic Obstructive Pulmonary Disease**

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Abstract

This study assessed functional balance among older adults at all COPD grades and explored balance impairment predictors. A cross-sectional study with outpatients with COPD (n=160; 72.2±7.9yrs; FEV₁63.8±23.7% predicted) was conducted. The Timed Up and Go (TUG) test was used to assess functional balance. Functional balance impairment was defined as a TUG score exceeding the upper limit of the confidence intervals of normative values for healthy older adults. Participants performed the TUG test in 11.0±4.8seconds. Functional balance impairment was present in 44.4% of the participants and was significantly more frequent in severe-to-very-severe COPD (62.5%). Body mass index (OR 1.12), number of medications (OR 1.20), restriction in recreational activities (OR 1.66) and depression score (OR 1.14) were multivariate predictors of functional balance impairment. Functional balance impairment is present at early COPD, although more evident at advanced grades. These findings highlight the importance of balance assessment in older patients at all COPD grades.

Keywords: Aging; chronic obstructive pulmonary disease; functional balance.

1 Falls are a worldwide major issue that have considerable negative consequences on
2 older adults' quality of life, such as decreased functional independence, social interaction and
3 life expectancy (Roe et al., 2009; World Health Organization, 2007). Furthermore, falls have
4 a considerable impact on healthcare systems, since the costs related to fall-related injuries are
5 substantial (Stevens, Corso, Finkelstein, & Miller, 2006; World Health Organization, 2007).
6 Evidence has shown that the risk of falling in older adults is multifactorial, relying on
7 biological, psychological, behavioral, environmental and socioeconomic factors (World
8 Health Organization, 2007). Nevertheless, impaired balance is one of the most important
9 predictors of falls (Muir, Berg, Chesworth, Klar, & Speechley, 2010). Therefore, research has
10 been undertaken to investigate balance impairment in different populations (Baetens, De
11 Kegel, Calders, Vanderstraeten, & Cambier, 2011; Norén, Bogren, Bolin, & Stenström, 2001;
12 Ryan, McCloy, Rundquist, Srinivasan, & Laird, 2011).

13 Chronic obstructive pulmonary disease (COPD) is one of the most prevalent chronic
14 diseases among adults aged 60 and older (Gershon, Warner, Cascagnette, Victor, & To,
15 2011). This chronic disease, despite being primarily characterized by progressive airflow
16 limitation, is known by its systemic features, such as impaired mobility and muscle weakness,
17 that contribute to high disability (The Global Initiative for Chronic Obstructive Lung Disease,
18 2013). These systemic features, together with the normal modifications associated with the
19 ageing process and the propensity to suffer from other co-morbidities, such as osteoporosis,
20 may predispose older adults with COPD to balance impairment and subsequent injuries.
21 Smith et al. found that older adults with COPD had reduced control of balance when
22 compared with matched healthy peers (Smith, Chang, Seale, Walsh, & Hodges, 2010).
23 Beauchamp et al. showed that 36% of the older adults with COPD were at risk of falling
24 (Beauchamp, Hill, Goldstein, Janaudis-Ferreira, & Brooks, 2009). More recently, a study by
25 Roig et al. reported that 31.7% of the older adults with COPD fall at least once during a 6-

1 months period (Roig, Eng, MacIntyre, Road, FitzGerald, et al., 2011). These studies
2 demonstrated that older adults with COPD present deficits in balance; however, they assessed
3 mainly patients with severe airflow limitation (forced expiratory volume in one second
4 (FEV_1) <50% predicted) (The Global Initiative for Chronic Obstructive Lung Disease, 2013).
5 Since evidence shows that physical activity levels and quadriceps strength are already
6 impaired at early COPD ($FEV_1 \geq 50\%$) (Gouzi et al., 2011; Shrikrishna et al., 2012), it can be
7 hypothesized that balance is impaired in these patients as well. Therefore, the main aim of this
8 study was to assess functional balance among older adults with different levels of COPD
9 severity and explore the predictors of functional balance impairment.

10 **Methods**

11 **Study design and participants**

12 A cross-sectional study with a convenience sample of outpatients with COPD was
13 conducted from November 2010 to June 2012 in the central region of Portugal. The study
14 received full approval from the Institutional Ethics Committee. Patients were recruited from
15 two primary care centers and one district hospital. Inclusion criteria were diagnosis of COPD
16 according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria,
17 clinical stability for 1 month prior to the study (no hospital admissions or exacerbations), age
18 ≥ 60 years old, ability to understand the purpose of the study and voluntarily consent to
19 participate. Patients were excluded if they were institutionalized (i.e., living in an institution
20 where formal care is provided), presented severe neurological, musculoskeletal and
21 psychiatric impairments and/or inability to understand and co-operate.

22 Patients with regular appointments in the institutions involved were identified via
23 clinicians. Eligible patients were contacted via telephone by clinic secretaries, who explained
24 the purpose of the study and asked about their willingness to participate. When patients
25 agreed to participate, an appointment with the researchers was scheduled in patients'

1 reference primary care center or hospital, to provide detailed information about the study.

2 Written informed consent was obtained prior to any data collection.

3 **Data collection procedures**

4 Socio-demographic data (gender, age, academic qualifications and occupation
5 situation) were first collected. Secondly, patients were asked about medication, oxygen use,
6 co-morbidities, hospitalization history in the preceding year and their perception of lack of
7 energy, dyspnea and restriction in recreational activities. Then, the Modified British Medical
8 Research Council (mMRC) questionnaire and the Hospital Anxiety and Depression Scale
9 (HADS) were filled in and finally, a physical exam was performed, which included the
10 assessment of: i) height and weight (measured using a calibrated digital scale); ii) lung
11 function and iii) functional balance. All assessments were performed by the same
12 physiotherapist, an external element of the medical teams and unknown to the patients. The
13 order of data collection was standardized for all patients.

14 **Measures**

15 **Perception of lack of energy, dyspnea and restriction in recreational activities.** To
16 assess the perception of lack of energy, dyspnea and restriction in recreational activities, the
17 International Classification of Functioning, Disability and Health (ICF) categories b130
18 Energy and drive functions, b460 Sensations associated with cardiovascular and respiratory
19 functions and d920 Recreation and leisure were used (Stucki et al., 2004). The extent of
20 patients' impairment was quantified on a 0 to 4 qualifier scale, which corresponds to no, mild,
21 moderate, severe and complete impairment, respectively (World Health Organization, 2001).
22 Patients were asked to choose a qualifier that best described their impairment/limitation.

23 **Modified British Medical Research Council questionnaire.** Patients were asked to
24 report their disability resulting from breathlessness using the mMRC questionnaire (Doherty
25 et al., 2006). The mMRC questionnaire comprises five grades (range 0–4), with higher grades

1 indicating greater perceived respiratory disability. This questionnaire is simple to administer
2 and correlates significantly with measures of health status (The Global Initiative for Chronic
3 Obstructive Lung Disease, 2013).

4 **Hospital Anxiety and Depression Scale.** The Portuguese version of the HADS was
5 used to assess anxiety and depression symptoms (Pais-Ribeiro et al., 2007). The HADS
6 contains 14 items, 7 measuring anxiety symptoms and 7 depressive symptoms (Zigmond &
7 Snaith, 1983). Each item is scored from 0 to 3 points, depending on the severity of the
8 symptoms therefore, the possible scores range from 0 to 21 for anxiety and 0 to 21 for
9 depression (Pais-Ribeiro et al., 2007). This scale has been used widely in patients with COPD
10 and has good reliability and validity (Bjelland, Dahl, Haug, & Neckelmann, 2002).

11 **COPD severity.** A spirometric test, using a portable spirometer (MicroLab 3500,
12 CareFusion, Kent, UK), was performed in all patients according to the American Thoracic
13 Society/European Respiratory Society Task Force standardization of lung function testing
14 (Miller et al., 2005). The classification of the COPD severity was carried out in accordance
15 with the GOLD criteria: “mild COPD = $FEV_1 \geq 80\%$ predicted”; “moderate COPD =
16 $50\% \leq FEV_1 < 80\%$ predicted”; “severe and very severe COPD = $FEV_1 < 50\%$ predicted” (The
17 Global Initiative for Chronic Obstructive Lung Disease, 2013).

18 **Exacerbation risk.** The exacerbation risk was assessed in accordance with the GOLD
19 criteria (The Global Initiative for Chronic Obstructive Lung Disease, 2013), which combines
20 COPD severity and mMRC score: Group A – low risk, less symptoms (mild or moderate
21 COPD and mMRC grade 0-1); Group B – low risk, more symptoms (mild or moderate COPD
22 and mMRC grade ≥ 2); Group C – high risk, less symptoms (severe to very severe COPD and
23 mMRC grade 0-1); and Group D – high risk, more symptoms (severe to very severe COPD
24 and mMRC grade ≥ 2).

1 **Timed Up and Go Test.** The Timed Up and Go (TUG) is one of the most suitable
2 performance measures for evaluating balance in community-dwelling older people (Lin et al.,
3 2004). This test was used to assess functional balance as recent research has suggested that
4 assessment of balance under multi-task conditions may be a more sensitive indicator of
5 balance problems than assessment of balance in a single-task context (Shumway-Cook,
6 Brauer, & Woollacott, 2000). The test requires the patient to rise from a standard chair, walk
7 3 meters, turn around, walk back to the chair, and sit down, after the command “go”
8 (Podsiadlo & Richardson, 1991). Patients were instructed to walk quickly, but as safely as
9 possible. Two TUG tests were performed and the best performance was considered. Patients
10 who usually used walking aids at home were recommended to use it during the test.
11 Normative reference values (mean and 95% confidence interval – 95%CI) for the TUG test in
12 healthy older adults are established for three age groups: 60 to 69 years old (8.1 seconds;
13 95%CI=7.1-9.0); 70 to 79 years old (9.2 seconds; 95%CI=8.2-10.2) and for 80 to 99 years old
14 (11.3 seconds; 95%CI =10.0-12.7) (Bohannon, 2006). Although these reference values were
15 obtained through a meta-analysis of studies with different methodologies, the data from
16 studies were found to be homogeneous. Therefore, these reference scores provide a
17 reasonable estimate of normal TUG performance. Functional balance impairment in this study
18 was defined as a TUG score exceeding the upper limit of the confidence intervals of
19 normative reference values for healthy older adults (i.e., 9.0 seconds for 60-69 years old, 10.2
20 seconds for 70-79 years old and 12.7 seconds for 80-99 years old).

21 **Statistical analysis**

22 Descriptive statistics were used to describe i) the socio-demographic and clinical
23 characteristics of the sample and ii) the TUG scores. For each age group (60-69, 70-79, 80-
24 99), the TUG scores were compared with the mean reference value from healthy older adults
25 using one-sample t-tests. Socio-demographic and clinical variables of patients with functional

1 balance impairment were compared with patients with no functional balance impairment
2 using independent t-tests for normally distributed data, Mann-Whitney U-tests or Kruskal
3 Wallis tests for non-normally distributed data and ordinal data, and Chi-square tests for
4 categorical data. The variables that were statistically different between these two groups were
5 used in a multivariate logistic regression. The level of significance considered was 0.05.
6 Statistical analyzes were performed using PASW Statistics (Predictive Analytics Software)
7 version 18.0 for Windows (SPSS Inc., Chicago, Illinois) and figures were created using
8 GraphPad Prism 5.0 (GraphPad Software, Inc., La Jolla, CA).

9 **Results**

10 **Participants**

11 A total of 169 patients were contacted however, 7 did not want to participate and 2 did
12 not complete the assessment. Therefore, 160 participants (102 males) enrolled in the study.
13 According to the GOLD classification, 33.1% participants had mild COPD (n=53;
14 70.1±8.4years old; FEV₁ 90.8±7.4% predicted), 36.9% moderate (n=59; 73.0±7.8years old;
15 FEV₁ 64.0±8.6% predicted) and 30% severe to very severe (n=48; 73.3±7.4years old; FEV₁
16 35.5±9.0% predicted). Most participants were married (n=121; 75.6%), finished the primary
17 school (n=105; 65.6%) and were currently retired (n=142; 88.8%). Regarding the
18 exacerbation risk, more than half of the participants (n=91; 56.8%) belonged to group B (low
19 risk, more symptoms). Table 1 provides the socio-demographic and clinical characteristics of
20 the participants.

21 *(insert table 1 about here)*

22 **TUG scores**

23 On average, participants performed the TUG test in 11.0±4.8 seconds. As shown in
24 fig. 1, the mean TUG score was significantly higher in participants with severe to very severe

1 COPD ($13.0 \pm 5.3s$) compared with participants with mild ($9.7 \pm 4.3s$; $p=0.001$) and moderate
2 ($10.5 \pm 4.3s$; $p=0.01$) COPD.

3 *(insert figure 1 about here)*

4 Figure 1: TUG scores of participants with COPD according to their grades. Box plots show
5 the median, interquartile range and extreme cases of individual variables. Significant
6 differences are identified with * ($p<0.05$).

7 Participants' TUG scores increased significantly with age ($p=0.001$). There was a
8 statistically significant difference in scores between patients with COPD over 69 years of age
9 and the normative reference values published by Bohannon (2006) ($p<0.05$), but no difference
10 was found for patients with COPD aged between 60 and 69 years ($p=0.085$; Fig. 2).

11 *(insert figure 2 about here)*

12 Figure 2: Comparison between the TUG scores of the participants in this study (mean and
13 95% confidence interval) and the reference values from healthy older adults from 60 to 99
14 years (mean and 95% confidence interval)(Bohannon, 2006). The squares represent data from
15 this study and the circles the normative reference scores. Significant differences are identified
16 with * ($p<0.05$).

17 Functional balance impairment, defined as a TUG score exceeding the upper limit of
18 the confidence intervals of normative references values for healthy older adults, was present
19 in 44.4% ($n=71$) of the sample. According to the GOLD grade, the prevalence of functional
20 balance impairment was higher in participants with severe to very severe COPD ($n=30$;
21 62.5%) compared to those with mild ($n=18$; 36.7%; $p=0.015$) and moderate ($n=23$; 36.5%;
22 $p=0.008$) COPD. Comparing participants with functional balance impairment with those with
23 no functional balance impairment, statistically significant differences were found for gender
24 ($p=0.038$), body mass index (BMI) ($p=0.001$), FEV₁ % predicted ($p=0.009$), number of
25 medications ($p=0.003$), oxygen use ($p=0.005$), hospitalizations history in the preceding year

1 (p=0.009), mMRC score (p=0.001), perception of lack of energy (p=0.001), dyspnea
2 (p=0.001), restriction in recreational activities (p=0.001), anxiety (p=0.005) and depression
3 scores (p=0.001) (table 2).

4
(insert table 2 about here)

5 A multivariate logistic regression was performed using the variables from table 2 with
6 probability values of $p < 0.05$. BMI (OR 1.12; 95% CI=1.03-1.22; $p=0.007$), number of
7 medications (OR 1.20; 95% CI=1.01-1.42; $p=0.041$), restriction in recreational activities
8 (OR 1.66; 95% CI=1.21-2.27; $p=0.002$) and depression score (OR 1.14; 95% CI=1.02-1.26;
9 $p=0.018$) were significantly associated with functional balance impairment. This regression
10 model predicted 31.6% of total variation of functional balance impairment.

11

Discussion

12 According to our knowledge, this was the first study to investigate functional balance
13 impairment in older adults at early and advanced COPD. The main findings of this study
14 were: i) that functional balance impairment is already observed in patients with early COPD
15 and ii) BMI, number of medications, restriction in recreational activities and depression score
16 are significant predictors of functional balance impairment in older adults with COPD.

17 On average, participants performed the TUG test in 11.0 ± 4.8 seconds, exceeding the
18 reference mean score (9.4 seconds) (Bohannon, 2006). However, previous studies in patients
19 with COPD found higher mean TUG scores than those identified in the present study
20 (15.4 ± 4.3 seconds (Beauchamp et al., 2009) and 15.7 ± 5.3 seconds (Beauchamp, O'Hoski,
21 Goldstein, & Brooks, 2010)). This difference may be explained by the different characteristics
22 of the samples included, since these studies included patients with moderate to very severe
23 COPD ($n=39$; mean FEV_1 of $41.5 \pm 17.0\%$ and $n=29$; $46.3 \pm 22.3\%$ predicted, respectively),
24 whereas our study also included patients with mild disease (mean FEV_1 of $63.8 \pm 23.7\%$
25 predicted). The mean TUG score was significantly different among COPD grades, where

1 patients with severe and very severe COPD achieved higher scores (13.0 ± 5.3 seconds; $n=48$).
2 A sub-group analysis has not been previously performed and therefore a comparison cannot
3 be made. Nevertheless, this finding was expected due to the progressive nature of COPD.
4 Even in participants with mild COPD (9.7 ± 4.3 seconds; $n=53$) the mean TUG score was
5 slightly above the established mean reference score (9.4 seconds) (Bohannon, 2006). These
6 results suggest that some patients with COPD, even at earlier grades, present functional
7 balance impairment when compared to age-matched healthy peers.

8 Pulmonary rehabilitation, a recommended standard of care in the management of
9 patients with COPD (Nici et al., 2006), does not include a specific component of balance
10 training, contributing only slightly to balance improvement (Beauchamp et al., 2010).
11 Therefore, it may be relevant to analyze the effect of incorporating balance training in
12 pulmonary rehabilitation. The inclusion of the thematic of falls in the psychoeducational
13 component of pulmonary rehabilitation programs, where strategies to prevent falling could be
14 discussed (e.g., the identification and avoidance of environmental hazards), should also be
15 considered.

16 In total, 44.4% ($n=71$) of the sample had functional balance impairment. It is difficult
17 to compare this result with previous work as designs and measures used differed. Eisner et al.
18 found that patients with moderate COPD ($n=1202$) performed significantly worse on
19 Functional Reach Test and on a tandem stance task compared with a control group (Eisner et
20 al., 2008). In another study, Roig et al., using the Sensory Organization Test, reported that
21 patients with COPD ($n=20$) exhibited marked deficits in postural control, compared to
22 controls (Roig, Eng, MacIntyre, Road, & Reid, 2011). Also Beauchamp et al. identified
23 significantly lower scores on the Balance Evaluation Systems Test in patients with severe
24 COPD ($n=37$) compared to aged matched healthy controls (Beauchamp et al., 2012). These
25 studies, confirm that patients with COPD have balance impairments, but also show the lack of

1 standardization in balance assessment. These findings highlight the need to identify in future
2 research the most appropriate static and dynamic tests to be used in the assessment of balance
3 in this population, allowing comparisons between different studies.

4 The second purpose of this study was to explore the predictors of functional balance
5 impairment. Female gender, airflow obstruction, oxygen use, hospitalization history in the
6 preceding year and mMRC were associated with functional balance impairment in older
7 adults with COPD, however, these variables were not retained in the multivariate regression
8 model. BMI, as well as the number of medications, were significant in the multivariate
9 regression model. A higher BMI was associated with functional balance impairment (OR
10 1.12). In a study from Roig et al. with patients with COPD (n=101) a difference in BMI
11 between fallers (27.9 Kg/m²) and non-fallers (24.9 Kg/m²) was found, although not
12 statistically significant(Roig, Eng, MacIntyre, Road, FitzGerald, et al., 2011). The assessment
13 of BMI, already recommended by the GOLD guidelines(The Global Initiative for Chronic
14 Obstructive Lung Disease, 2013), is therefore important to consider when assessing balance
15 impairment in patients with COPD. As expected, the number of medication intake (OR 1.20)
16 was an important predictor of functional balance impairment. Recent studies corroborate these
17 findings (Gnjidic et al., 2012; Lawlor, Patel, & Ebrahim, 2003), suggesting that regular
18 medication reviews may be a useful strategy to reduce falls in this population.

19 Restrictions in recreational activities (OR 1.66) and depression (OR 1.14) were also
20 retained in the multivariate model. These results reinforce the importance of considering the
21 impact of the disease in patients' lives when assessing balance in this population, and not only
22 the lung function impairment. It has been previously observed that fear of falling in patients
23 with COPD was associated with increased levels of depression (Hellström, Vahlberg, Urell, &
24 Emtner, 2009). A previous study using data from 4050 older women found that depression
25 was associated with about a twofold increased risk of falling(Lawlor et al., 2003). This

1 relationship is not well explored; however, the use of antidepressant medications and
2 inattention to the environment have been reported as potential explanations (Rubenstein &
3 Josephson, 2006). Therefore, it is important to consider the screening of depression symptoms
4 in the comprehensive assessment of patients with COPD as it can be a helpful strategy in the
5 prevention of falls among this population.

6 A number of limitations of this study need to be acknowledged. First, since
7 institutionalization was an exclusion criterion, only older adults who were living in the
8 community were included and therefore our data may not be representative of the general
9 population with COPD. Future studies should also analyze balance in institutionalized
10 patients with COPD. Secondly, balance in this study was assessed using the TUG, a
11 functional balance test. In future work, the inclusion of other balance measures and the
12 assessment of lower-extremity strength and exercise tolerance would be beneficial to better
13 understand this issue in this population. Another potential limitation of the study might be the
14 comparison of our results with established normative reference values from healthy older
15 adults (Bohannon, 2006). These reference values were obtained through a meta-analysis of
16 heterogeneous studies however, the data from studies were found to be homogeneous. Thus, it
17 is believed that the conclusions from this study can be drawn with confidence. However, in
18 future studies, a control group with healthy subjects with similar demographic characteristics
19 could also be included.

20 **Conclusions**

21 Older patients with COPD, independently of their GOLD grade, have functional
22 balance impairment. Patients with higher BMI, number of medications, restriction in
23 recreational activities and depression score are those with higher probability of having
24 functional balance impairment. These findings highlight the importance of screening for
25 functional balance impairments in the comprehensive assessment of older patients with

1 COPD. Future research is needed to investigate the role of balance training and fall
2 prevention strategies as part of pulmonary rehabilitation programs in order to prevent falls in
3 older patients with COPD.

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8 **Conflict of interest**

9 The authors have no conflict of interest.

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1 **Table 1 Socio-demographic and clinical characteristics of the participants (n=160).**

Characteristics	Mild COPD (n=49)	Moderate COPD (n=63)	Severe to very severe COPD (n=48)	Total (n=160)
Age (years)	70.1±8.4(60-88)	73.0±7.8(61-93)	73.3±7.4(60-88)	72.2±7.9(60-93)
Male	25(51%)	41(65.1%)	36(75%)	102(63.8%)
Marital status				
Married	32(65.3%)	50(79.4%)	39(81.2%)	121(75.6%)
Widowed	11(22.5%)	10(15.9%)	7(14.6%)	28(17.5%)
Divorced	5(10.2%)	1(1.6%)	1(2.1%)	7(4.4%)
Single	1(2.0%)	2(3.1%)	1(2.1%)	4(2.5%)
Academic qualifications				
Primary school	29(59.2%)	42(66.7%)	34(70.8%)	105(65.6%)
Secondary school	13(26.5%)	16(25.4%)	14(29.2%)	43(26.9%)
High school	4(8.2%)	4(6.3%)	-	8(5%)
University	3(6.1%)	1(1.6%)	-	4(2.5%)
Current occupation				
Retired	43(87.8%)	54(85.7%)	45(93.8%)	142(88.8%)
Employed	3(6.1%)	6(9.5%)	1(2.1%)	10(6.3%)
Unemployed	3(6.1%)	3(4.8%)	2(4.1%)	8(5%)
BMI (Kg/m ²)	28.3±4.9(19-45)	28.4±4.5(19-40)	26.3±4.2(18-38)	27.8±4.6(18-45)
mMRC	M 3 IQR 1	M 3 IQR 1	M 4 IQR 1	M 3 IQR 2
FEV ₁ (% predicted)	90.8±7.4(79-110)	64.0±8.6(50-79)	35.5±9.0(16-49)	63.1±23.0(16-110)
Exacerbation risk				
A	9(17%)	12(20.3%)	-	21(13.1%)
B	44(83%)	47(79.7%)	-	91(56.8%)
C	-	-	2(4.2%)	2(1.3%)
D	-	-	46(95.8%)	46(28.8%)

2 Note: values show mean±SD or n(%) unless otherwise indicated. Abbreviations: BMI, body
3 mass index; mMRC, Modified British Medical Research Council questionnaire; M, median;
4 IQR, interquartile range; FEV₁, forced expiratory volume in one second.

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1 **Table 2 Characteristics of the participants with no functional balance impairment and**
 2 **with functional balance impairment (n=160).**

	No functional balance impairment (n=89)	Functional balance impairment (n=71)	p-value
Female	26(29.2%)	32(45.1%)	0.038*
Age (years)	72.0±8.2	72.6±7.6	0.651
BMI (Kg/m ²)	26.7±3.8	29.0±5.2	0.001*
Living alone	10(11.2%)	11(15.5%)	0.408
FEV ₁ (% predicted)	68.3±22.6	58.1±23.9	0.009*
Medications	3.8±2.0	5.1±2.6	0.003*
Oxygen use	2(2.2%)	10(14.1%)	0.005*
Comorbidities	M 2 IQR 2	M 2 IQR 2	0.947
Hospitalizations	6(6.7%)	15(21.1%)	0.009*
mMRC	M 2 IQR 1	M 3 IQR 2	0.001*
Lack of energy	M 0 IQR 1.5	M 1 IQR 3	0.001*
Dyspnea	M 2 IQR 1	M 3 IQR 2	0.001*
Restriction in recreation	M 0 IQR 2	M 2 IQR 3	0.001*
Anxiety score	7.2±4.0	9.1±4.4	0.005*
Depression score	6.6±3.5	8.9±3.8	0.001*

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 4 Note: values show mean±SD or n(%) unless otherwise indicated. Abbreviations: BMI, body
 5 mass index; FEV₁, forced expiratory volume in one second; mMRC, Modified British
 6 Medical Research Council questionnaire; M, median; IQR, interquartile range. *Significant at
 p<0.05.

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