



Postural balance in COPD with obstructive sleep apnoea: a cross-sectional study

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Individuals with COPD with moderate and severe OSA present significant changes in the postural balance and increased recurrence of fall compared with those with no OSA. This study helps to understand these individuals better. <https://bit.ly/30KeYJF>

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Abstract

Objective The aim of this study was to assess the postural balance in COPD patients with obstructive sleep apnoea (OSA). Physical activity, anxiety and depression symptoms, mood, and falls were also assessed in this population.

Methods Moderate to severe COPD patients were assessed for laboratory and clinical postural balance (force platform and mini-balance evaluation systems test (Mini-BESTest)), physical activity (accelerometry), OSA (polysomnography), sleep quality (Pittsburgh Sleep Quality Index), sleepiness (Epworth Sleepiness Scale), anxiety and depression symptoms (Hospital Anxiety and Depression Scale), dyspnoea (modified Medical Research Council), clinical status (COPD Assessment Test) and mood (Brunel Mood Scale). Self-reported falls were recorded for 6 months *via* phone calls.

Results COPD patients (n=70) were divided according to the polysomnography findings into the no OSA (n=30), mild OSA (n=25), and moderate to severe OSA (n=15) groups. Compared to patients with no OSA, those with moderate to severe OSA (msOSA group) presented median (interquartile range) increased path length (30.5 (23.9–34.5) cm *versus* 39.0 (30.6–52.6) cm, anteroposterior displacement (1.89 (1.39–2.31) cm *versus* 2.54 (2.06–2.83) cm and postural adjustment velocity (1.02 (0.80–1.15) cm·s⁻¹ *versus* 1.30 (1.02–1.76) cm·s⁻¹) (p<0.05). No differences were observed in the Mini-BESTest scores among the groups. The msOSA group presented a greater number of recurrent fallers in the first follow-up trimester. No association was observed between postural balance and age and pulmonary function

Conclusion Individuals with COPD and moderate to severe OSA present changes in postural balance, including broader oscillation, faster postural adjustments and a greater risk of falls than those with no OSA. Physical activity, anxiety and depression symptoms, and mood are similar between COPD patients with and without OSA.

Introduction

COPD is a preventable and treatable respiratory disease characterised by persistent respiratory symptoms and airflow limitation due to airway and/or alveolus abnormalities [1]. COPD prevalence is high and has been increasing substantially with the ageing population [1, 2]. According to the World Health Organization, COPD is the third leading cause of death worldwide, causing 3.2 million deaths in 2019, and mainly affects the elderly in low- and middle-income countries [3]. COPD is considered a complex and multicomponent disease characterised by chronic systemic inflammation that coexists with cardiovascular, skeletal and nutritional disorders, impaired postural balance, increased risk of falls [4] and sleep disorders [5].



Obstructive sleep apnoea (OSA) affects ~10–30% of COPD patients [5]. It can lead to physiological and biological disturbances, including hypoxaemia, hypercapnia, changes in systemic haemodynamics, cerebral disease and sleep deprivation [6, 7]. Furthermore, there is growing evidence that COPD patients have a high prevalence of other sleep disorders, including decreased sleep efficiency, prolonged time to fall asleep, reduced total sleep time and increased wakefulness frequency [8]. These disorders can lead to daytime sleepiness, increased exacerbations, mortality [9] and greater use of health resources [10].

Impaired postural balance is also prevalent in patients with COPD [11]. Postural balance is defined as the ability to control the body position in space, keeping the centre of body gravity within the limits of the supporting base in static and dynamic positions [12]. Previous studies demonstrated significant balance deficits in COPD patients compared to healthy individuals, and the former tend to exhibit impaired balance reactions in response to externally applied disturbances [13, 14]. BEAUCHAMP *et al.* [14] showed that COPD patients have a delayed reaction time for balance response associated with reduced muscle strength and physical activity levels. Moreover, worsening of postural balance is frequently observed when they perform dynamic activities, resulting in harmful effects on their functionality [15, 16]. A growing body of evidence has recently shown that COPD patients present balance deficits that cannot be explained by age-related processes alone [17]. Increased comorbidities, dyspnoea, physical inactivity, muscle weakness and reduced balance confidence have been reported as possible factors causing frequent falls in COPD patients [18–20].

Although several postural changes in COPD individuals have been described, the prevalence of OSA in this population remains poorly known. In individuals without respiratory diseases, there is evidence that postural stability is worse in individuals with OSA [21], and this sleep disorder is associated with fall risk [22]. The authors support this effect because OSA impairs various physiological functions and systems important for balance and posture control, including the vestibular system, visual acuity and cognitive function [22].

Several studies have demonstrated that COPD patients may have sleep and postural balance disorders; however, the interaction between these two comorbidities has not been elucidated. The present study hypothesised that COPD individuals with OSA have worse postural balance, greater risk of falls and symptoms of anxiety and depression, lower physical activity, and longer sedentary behaviour than those without OSA.

This study aimed to assess the static postural balance in COPD patients with OSA. The secondary aim was to evaluate the physical activity levels, sedentary time, anxiety and depression symptoms, mood, and falls between COPD patients with and without OSA.

Methods

Participants

This study included individuals with moderate to severe COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [1] and undergoing medical treatment at the Clinics Hospital at University of Sao Paulo. Individuals were recruited from January 2020 to December 2021 and were informed about the study objectives and procedures; only those who signed the informed consent form were included. Inclusion criteria were age ≥ 50 years, tobacco history of ≥ 10 pack-years, no pulmonary rehabilitation in the last 6 months and clinical stability. Clinical stability in COPD patients may vary from 3 to 4 weeks according to the literature in studies involving sleep disorders [23], assessment of postural balance [16] and physical activity [24]. If patients were exacerbated during the visit period, they were medicated and initiated the evaluations after 4 weeks. The criteria for ineligibility included the use of oral corticosteroids, use of continuous positive airway pressure (CPAP) at night, previously diagnosed OSA, oxygen dependency, musculoskeletal limitations or neurological conditions that prevented assessments, uncorrected vision abnormalities (as low visual acuity or visual loss), hearing deficit and difficulty in understanding the evaluations. The study followed the principles of the Declaration of Helsinki, and the Hospital Ethics Committee approved the study (approval number: 29469320.3.0000.0068).

Experimental design

In this cross-sectional study, assessments were performed during two hospital visits at an interval of 7 days (figure 1). During the first visit, the patients were assessed for anthropometric data, comorbidities (Charlson comorbidity index), lung function (spirometry) recorded in the last 6 months in medical records, sleep quality (Pittsburgh Sleep Quality Index (PSQI)) and sleepiness (Epworth Sleepiness Scale (ESS)). Then, patients underwent type I polysomnography (PSG) examination and were given an accelerometer before returning for the second visit. During the second visit, the participants underwent assessments for laboratory postural balance (force platform and clinical Mini-Balance Evaluation Systems Test (Mini-BESTest)),

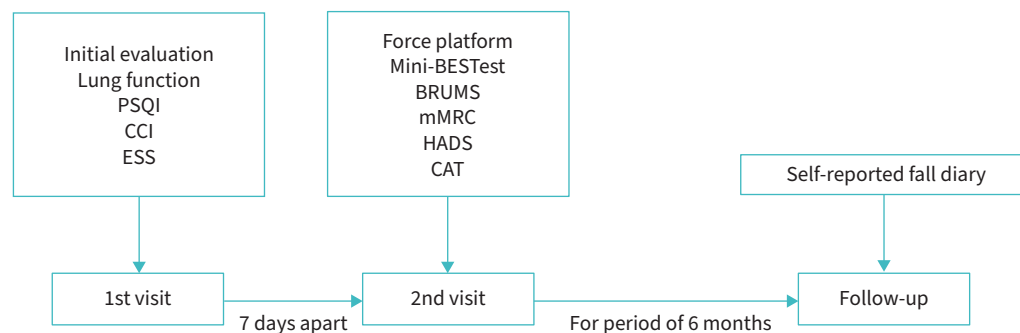


FIGURE 1 Study flow diagram. PSQI: Pittsburgh Quality Index; CCI: Charlson Comorbidity Index; ESS: Epworth Sleepiness Scale; Mini-BESTest: Mini-balance Evaluation Systems Test; BRUMS: Brunel Mood Scale; mMRC: modified Medical Research Council dyspnoea scale; HADS: Hospital Anxiety and Depression Scale; CAT: COPD Assessment Test.

dyspnoea (modified Medical Research Council (mMRC) scale), health-related quality of life (COPD Assessment Test (CAT)), anxiety and depression symptoms (Hospital Anxiety and Depression Scale (HADS)) and mood (Brunel Mood Scale (BRUMS)). Falls were evaluated monthly using a 6-month self-reported falls diary during the follow-up period.

Outcomes

Comorbidities

Comorbid conditions were categorised using the original Charlson index as described by CHARLSON *et al.* [25]. It considers 19 different comorbidities, each classified with a score of 1–6 points based on the adjusted relative risk of 1-year mortality, with a total score range of 0–37.

Type I PSG exam

The monitors to assess sleep disorders are classified as type I to IV. PSG is a type I device, and the test is performed in a laboratory, while types II to IV use portable sleep monitors for home sleep apnoea testing. In addition, type I PSG is considered the current “gold standard” for diagnosing OSA [26]. The standard montage was used, including an electroencephalogram (EEG) with central (C) and occipital (O) channels referred to the auricular channel (A) (C3/A2, C4/A1, O1/A2 and O2/A1), electro-oculogram, submental electromyogram (EMG), left and right anterior tibialis EMG, electrocardiogram, thoracoabdominal effort measurement, oronasal airflow measurement (thermistor and nasal pressure-based airflow measurement), pulse oximetry for oxygen saturation and body position sensor EMBLA S7000 (Embla Systems, Broomfield, CO, USA) or Alice 5 (Philips Respironics, Murrysville, PA, USA) [27]. A specialised technician monitored the PSG assembly throughout the night, and the medical team performed the examination.

OSA is characterised by a reduction in the airflow curve by $\geq 90\%$ lasting at least 10 s, and hypopnea is characterised by a respiratory event leading to a reduction in the airflow by $\geq 30\%$ for at least 10 s and associated with oxyhaemoglobin desaturation of at least 4% [27]. The apnoea–hypopnea index (AHI) criteria recommended and accepted by the American Academy of Sleep Medicine were used as follows: no OSA, AHI < 5 sleep events/hour; mild OSA, 5–15 sleep events/hour; moderate OSA, 15–30 sleep events/hour; and severe OSA, ≥ 30 sleep events/hour [27]. Based on the PSG findings, the participants were classified into the following three groups: no OSA, mild (mOSA), and moderate to severe OSA (msOSA).

Pittsburgh sleep quality index

The PSQI consists of 19 self-rated questions and five questions rated by the bed partner or roommate, and it evaluates the sleep quality and disorders in the last month. These questions assess several factors related to sleep quality, including sleep duration, latency estimates, and frequency and severity of specific sleep-related problems. The items are grouped into seven component scores, each weighted equally on a scale of 0–3. The seven component scores are then summed to yield a global PSQI score ranging from 0 to 2; higher scores indicate worse sleep quality [28].

Epworth Sleepiness Scale

The ESS is used to determine the degree of daytime sleepiness in adults. It is based on questions referring to eight situations, some known to be very soporific and others less so. The participants were asked to rate

on a scale of 0–3 how likely they were to doze off or fall asleep in the eight situations based on their usual way of life in recent times. If the patient had not been in these situations recently, they were asked to estimate how each might have affected them [29]. The cervical circumference measurement, the main predictor of OSA, was also performed; the normal values were 43 cm for men and 38 cm for women [30].

Laboratory postural balance test (force platform)

Postural balance data were acquired using AMTI AccuSway Optimized Balance Platform (Advanced Mechanical Technologies, Inc., Watertown, MA, USA). The centre of pressure (CoP) variables included path length, 95% ellipse area, mediolateral (CoP_{mi}) and anteroposterior (CoP_{ap}) displacements, and CoP mean speed. Three attempts were performed, and the mean value was considered for the analysis. The acquisition time for each attempt was 30 s, and the sampling frequency was 100 Hz. The platform was placed 1 m from the wall, where a figure was placed at each participant's eye level. The assessment was performed with the participant in a standing position and centred on the platform with the head and torso aligned, barefoot, and with plantar support in the natural position [31, 32]. After data collection, the variables were processed and calculated using Balance Clinic Software (Advanced Mechanical Technologies, Inc.). Data were filtered using a low-pass filter at 10 Hz.

Clinical postural balance test (Mini-BESTest)

The mini balance evaluation systems test (Mini-BESTest) comprises 14 items grouped into four domains as follows: anticipatory postural adjustments, postural responses, sensory orientation and gait. Each item is scored from 0 (unable or requiring help) to 2 (normal), with a total score of 28 points; higher scores indicate better balance performance [33].

Physical activity and sedentary time

Physical activity was defined according to the World Health Organization (WHO) guideline as any bodily movement produced by skeletal muscles that requires energy expenditure and participants reported whether or not they performed. [34] Movement behaviours were objectively measured using an accelerometer Actigraph GT3X (Actigraph, Pensacola, FL, USA). The device was initialised *via* a computer interface to collect data in 60-s epochs on the three axes using specific software (ActiLife 6.13.3 Firmware version). Participants wore the device on their waist (using an elastic belt) during wake time for 7 days consecutively. Data from the valid days (≥ 4 days and ≥ 10 h of recording) were presented as the mean number of steps per day, time spent in moderate–vigorous physical activity ($\text{min}\cdot\text{day}^{-1}$; defined as ≥ 1951 counts/min), and sedentary time ($\text{min}\cdot\text{day}^{-1}$; defined as < 100 counts/min) [35]. Participants logging $\geq 10\,000$, ≥ 7500 , and ≥ 5000 steps per day were classified as physically active, somewhat active and low-level active, respectively [36].

Dyspnoea symptoms

The mMRC dyspnoea scale, a simple, 5-point grading system, tests breathing problems during daily tasks. The final value determines the extent of the disability caused by dyspnoea [37].

Health-related quality of life

The CAT questionnaire consists of eight items (cough, phlegm, chest tightness, breathlessness, activity limitation, confidence in leaving home, sleep and energy) with scores of 0–5 for each severity item. These are then summed to give an overall score ranging from 0 (excellent perceived health) to 40 (worst health) [38].

Anxiety and depression symptoms

The HADS comprises two subscales for assessing anxiety (HADS-A) and depressive symptoms (HADS-D). Each subscale consists of seven items with a 4-point ordinal response format. Scores range from 0 to 21 for each subscale, with higher scores indicating higher levels of anxiety or depression. All participants answered each item based on how they felt and/or behaved during the past week [39].

Mood assessment

The BRUMS is a 24-item measure of mood that has been validated for use in a wide variety of populations. The scale consists of six subscales of tension, depression, anger, vigour, fatigue and confusion. Tension includes feeling nervous, anxious, worried or panicky. Depression includes feeling unhappy, miserable, depressed or downhearted. Anger includes feeling bitter, angry, annoyed or energetic. Vigour includes feeling energetic, active, lively or alert. Fatigue includes feeling exhausted, tired, worn out or sleepy. Finally, confusion includes feeling muddled, uncertain or confused. All the participants responded on a 5-point Likert scale (0=not at all, 1=little, 2=moderate, 3=quite a bit and 4=extreme), with total possible subscale scores in the range of 0–16 [40].

Falls

A fall is defined as “an unexpected event in which the participants come to rest on the ground, floor, or lower level” [41]. Every fall recorded in this study was followed by a telephone call by the same trained researcher who recorded the fall for consistency’s sake. This standardised interview was conducted via telephone calls to confirm fall occurrence and clarify the nature of the fall, as previously described [16]. In addition, they were asked if they underwent pulmonary rehabilitation, sleep treatment or oxygen use during the follow-up period. Patients who reported one or more falls during the follow-up period were referred to as “fallers”. Patients were classified as “recurrent fallers” if they reported two or more falls within 3 months during the 6-month follow-up period.

Statistical analysis

Sample size

The sample size of 69 patients for three groups was calculated based on a previous study showing a difference of 2.2 ± 3.0 cm in the length of CoP displacement [21]. In our study, the length of CoP displacement is referred to as the distance of trajectory (DOT). The α value was adjusted at 0.05 and the power at 0.80.

Descriptive analysis and normality of data

Descriptive data for the qualitative and quantitative variables are expressed as percentages and medians (interquartile range (IQR)), respectively. For continuous quantitative variables, data normality was tested using the Kolmogorov–Smirnov test. One-way analysis of variance (ANOVA) was used to compare the postural balance between the groups, followed by the Bonferroni *post hoc* or Kruskal–Wallis test followed by Dunn’s *post hoc* test. All analyses were performed using the statistical software GraphPad Prism (version 5.0; GraphPad Software, Inc., La Jolla, CA, USA) with a significance level of 5%.

Results

This study included 70 participants. In total, 791 individuals with moderate to severe COPD were screened in a tertiary hospital from January 2020 to December 2021. Of these, 660 individuals did not fulfil the

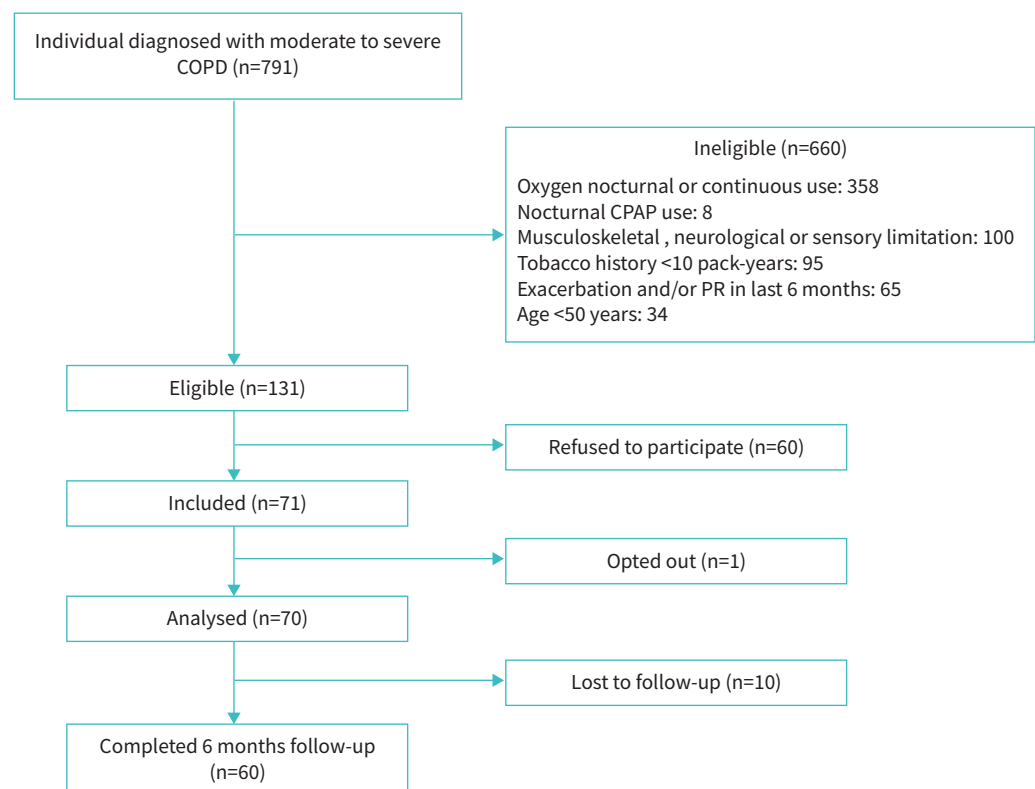


FIGURE 2 Flowchart of the participants through the study. COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure; PR: pulmonary rehabilitation.

inclusion criteria (358 using oxygen nocturnal or continuous, eight using CPAP at night, 100 had musculoskeletal, neurological or sensory limitations, 95 had a smoking history of <10 pack-years, 65 had one or more exacerbation(s) or underwent pulmonary rehabilitation in the last 6 months, and 34 were below 50 years of age) (figure 2). Additionally, of the eligible individuals, 60 refused to participate, and one withdrew during the protocol implementation (figure 2).

The anthropometric data are presented in table 1. Most of the patients were male (55.7%). Compared to the patients in the other groups, the msOSA group patients were older and had a higher cervical circumference. Individuals from the msOSA group presented a lower airway obstruction quantified by forced expiratory volume in 1 s (FEV₁) compared with the no OSA group (p<0.05; table 1). No inter-group differences were observed for professional status, comorbidities, dyspnoea, health-related quality of life, mood, physical activity level or clinical balance (table 1) and their four domains. The total HADS score was similar between the groups; however, the anxiety domain scores were higher in the no OSA group than in the msOSA group (median (interquartile range): 9.00 (5.75–11.25) versus 3.00 (1.00–9.00)). Table 2 shows the sleep variables evaluated by type I PSG. A greater minimum desaturation was observed in the mOSA and msOSA groups in relation to those with no OSA, as well as 4% oxygen desaturation index (ODI_{4%}) in the msOSA group in relation to the other two groups (p<0.05).

TABLE 1 Baseline characteristics of the participants

Outcomes	All participants	No OSA	Mild OSA	Moderate to severe OSA
Participants n	70	30	25	15
Demographic data				
Male	39 (55.7)	15 (50.0)	13 (52.0)	11 (73.3)
Age years	68.0 (62.7–72.2)	65.0 (60.5–70.2)	68.0 (64.0–71.0)	73.0 (67.0–74.0) [#]
BMI kg·m ⁻²	27.0 (23.4–30.2)	24.9 (22.6–30.2)	26.4 (23.0–29.3)	30.0 (27.0–32.1)
Cervical circumference cm	38.0 (35.0–41.0)	36.5 (32.0–40.0)	37.0 (35.0–41.0)	41.0 (38.0–44.0) [#]
Tobacco history				
Former smoker	64 (91.0)	27 (90.0)	24 (96.0)	13 (86.6)
Smoking pack-years	49.0 (30.0–80.0)	41.0 (30.0–67.2)	50.0 (37.5–80.0)	50.0 (30.0–90.0)
Pulmonary function				
FVC % of predicted	69.0 (57.0–79.2)	67.5 (56.7–78.0)	64.0 (55.0–77.0)	77.0 (67.0–85.0)
FEV ₁ % of predicted	42.5 (32.7–56.5)	37.0 (30.7–55.7)	42.0 (37.5–49.0)	55.0 (43.0–65.0) [#]
FEV ₁ /FVC ratio	0.51 (0.41–0.59)	0.46 (0.38–0.59)	0.53 (0.46–0.57)	0.59 (0.42–0.67)
Working status				
Retiree	48.0 (68.5)	20.0 (66.6)	18 (72.0)	10.0 (66.6)
Comorbidities				
CCI score	2.0 (1.00–3.00)	2.0 (1.00–3.00)	2.0 (1.00–4.00)	1.00 (1.00–2.00)
Number of comorbidities				
0 to 2	41.0 (58.5)	18.0 (60.0)	15.0 (60.0)	8.00 (53.4)
≥3	29.0 (41.5)	12.0 (40.0)	10.0 (40.0)	7.00 (46.6)
Dyspnoea/health status				
mMRC total score	2.00 (1.00–4.00)	2.00 (1.00–3.25)	2.00 (1.00–4.00)	2.00 (1.00–3.00)
0 to 2	40.0 (57.1)	18.0 (60.0)	13.0 (52.0)	9.00 (60.0)
3 to 4	30.0 (42.9)	12.0 (40.0)	12.0 (48.0)	6.00 (40.0)
CAT score	19.0 (14.0–23.0)	19.5 (15.5–22.2)	19.0 (15.0–24.5)	18.0 (13.0–21.0)
Anxiety/depression/mood				
HADS total score	14.0 (6.0–19.0)	16.5 (12.0–20.5)	10.0 (6.50–17.0)	7.00 (4.00–17.0)
BRUMS score	28.0 (19.0–39.0)	28.5 (18.2–40.7)	26.0 (21.0–40.0)	28.0 (13.0–39.0)
Physical activity				
Sedentary time h·day ⁻¹	739.0 (604.3–914.5)	756.0 (592.0–918.3)	740.0 (580.5–896.0)	705.0 (661.0–1065.0)
MVPA min·day ⁻¹	6.00 (2.00–13.0)	5.00 (1.00–12.2)	10.0 (3.50–17.0)	8.00 (2.00–11.0)
Steps-per day	4026 (2485–5438)	3830 (2007–5144)	4703 (3058–6967)	2789 (1815–5423)
Clinical balance				
Mini-BESTest total score	23.0 (20.0–25.0)	23.0 (20.7–25.0)	23.0 (18.5–25.0)	24.0 (22.0–26.0)

Data are presented as median (interquartile range) or n (%). No obstructive sleep apnoea group (AHI: <5 sleep events/hour); mild obstructive sleep apnoea group (AHI: 5 to 15 sleep events/hour); moderate to severe obstructive sleep apnoea group (AHI: ≥15 sleep events/hour). OSA: obstructive sleep apnoea; AHI: apnoea–hypopnea index; BMI: body mass index; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; CCI: Charlson Comorbidity Index; mMRC: modified Medical Research Council; CAT: COPD Assessment Test; HADS: Hospital Anxiety and Depression Scale; BRUMS: Brunel Mood Scale; MVPA: moderate–vigorous physical activity; Mini-BESTest: Mini-Balance Evaluation Systems test. #: p<0.05 between comparison no OSA and moderate to severe OSA groups.

TABLE 2 The sleep variables and medications in use of the participants

Outcomes	All participants	No OSA	Mild OSA	Moderate to severe OSA
Participants n	70	30	25	15
Sleep variables				
PSG				
AHI score	6.65 (2.30–13.8)	2.20 (1.20–3.30)	8.10 (6.85–11.4)	33.3 (21.6–46.4) [#]
Mean S _{pO₂} %	88.7 (86.2–90.8)	89.8 (87.4–91.8)	88.1 (85.7–89.7)	87.7 (84.2–89.7)
Minimum S _{pO₂} %	79.0 (74.0–83.2)	82.5 (79.5–86.2)	77.0 (73.5–81.5) [#]	74.0 (68.0–80.0) ⁺
NREM sleep stages				
N1+N2 %	76.8 (68.5–83.8)	76.8 (63.9–83.1)	72.8 (65.2–83.5) [§]	81.7 (78.2–86.8)
N3 %	9.00 (2.05–14.5)	9.75 (5.17–17.4)	10.7 (6.65–15.9) [§]	0.00 (0.00–10.5) ⁺
REM %	13.6 (9.57–19.5)	13.0(8.95–17.5)	14.4 (11.4–21.3)	15.2 (9.20–18.3)
SE %	84.9 (77.7–88.7)	84.2 (77.7–89.5)	85.9 (78.5–89.5)	84.7 (77.0–88.1)
AI events/hour	16.3 (13.0–24.3)	15.5 (12.4–20.1)	15.7 (11.3–19.7) [§]	29.2 (20.5–36.7) ⁺
ODI _{4%} events/hour	5.00 (2.00–12.0)	2.00 (1.00–3.70)	8.00 (5.55–10.4)	27.0 (18.0–39.0) [#]
TST min	355.3 (318.0–389.0)	354.5 (318.1–377.9)	343.5 (311.3–398.3)	371.5 (347.5–380.5)
TST S _{pO₂} <90%, %	72.4 (22.2–96.4)	44.1 (3.70–96.9)	84.8 (44.9–97.3)	76.1 (48.7–96.7)
PSQI score	10.0 (8.0–12.2)	10.0 (8.00–13.0)	10.0 (8.00–13.0)	8.00 (6.00–11.0)
ESS score	7.0 (3.75–11.2)	5.50 (2.27–9.25)	7.00 (5.00–12.5)	6.00 (2.00–12.0)
Medications in use				
Inhalation corticosteroid	61.0 (87.1)	26.0 (86.6)	23.0 (92.0)	12.0 (80.0)
β ₂ short duration	40.0 (57.1)	19.0 (63.3)	14.0 (56.0)	7.00 (46.6)
β ₂ long duration	63.0 (90.0)	27.0 (90.0)	22.0 (88.0)	14.0 (93.3)
Long-acting anticholinergic	52.0 (74.2)	23.0 (76.6)	19.0 (76.0)	10.0 (66.6)
Opioid	2.00 (2.86)	0.00 (0.00)	2.00 (8.00)	0.00 (0.00)
Benzodiazepine	1.00 (1.43)	0.00 (0.00)	1.00 (4.00)	0.00 (0.00)
Antidepressant	2.00 (2.86)	0.00 (0.00)	1.00 (4.00)	1.00 (6.66)
Calcium channel blockers	14.0 (20.0)	5.00 (16.6)	6.00 (24.0)	3.00 (20.0)

Data are presented as median (interquartile range) or n (%). AHI: apnoea–hypopnea index; no OSA: no obstructive sleep apnoea group (AHI: <5 sleep events/hour); mOSA: mild obstructive sleep apnoea group (AHI: 5 to 15 sleep events/hour); msOAS: moderate to severe obstructive sleep apnoea group (AHI: ≥15 sleep events/hour); PSG: polysomnography; S_{pO₂}: pulse oximeter oxygen saturation; NREM: non-rapid eye movement; REM: rapid eye movement; SE: sleep efficiency; AI: arousal index; ODI_{4%}: 4% oxygen desaturation index; TST: total sleep time; PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale. #: p<0.05 between comparison no OSA, mOSA and msOSA groups; #: p<0.05 between comparison no OSA and mOSA groups; +: p<0.05 between comparison no OSA and msOSA groups; §: p<0.05 between the comparison mOSA and msOSA groups.

Figure 3 shows the assessment of the initial CoP pattern of each group in static postural balance using a force platform. The CoP of the no OSA, mOSA and msOSA groups presented negative values on the y-axis (posterised position) (median (IQR): -1.07cm (-2.33 – -0.52), -1.61cm (-2.77 – -0.28) and -1.85cm (-2.86 – 0.40), respectively). Moreover, the postural balance varied according to the OSA severity. The CoP postural balance of the mOSA and msOSA groups presented a greater anteroposterior displacement (y-axis) than the no OSA group (figure 3).

The path length, mean postural speed, and CoP_{ml} and CoP_{ap} displacements are presented in figure 4a–d. The path length in the no OSA group was shorter than in the msOSA group (30.5 (23.9–34.5) cm *versus* 39.0 (30.6–52.6) cm; p<0.05) (figure 4a); however, no difference was observed between the mOSA group and the msOSA and no OSA groups. The velocity for postural adjustment was also greater in the msOSA group than in the no OSA group (1.30 (1.02–1.76) *versus* 1.02 (0.80–1.15) cm·s⁻¹; p<0.05) (figure 4b); however, no difference was observed between the mOSA group (1.03 (0.89–1.28) cm) and the no OSA and msOSA groups. The CoP_{ap} displacement was greater in the msOSA group than in the no OSA group (2.54 (2.06–2.83) cm *versus* 1.89 (1.39–2.31) cm; p<0.05) (figure 4d); no difference was observed between the mOSA group and the no OSA and msOSA groups. In contrast, no inter-group differences were observed in CoP_{ml} displacement (figure 4c). Even though the msOSA group patients were older and presented better lung function as compared to the patients of the other groups, no linear association was observed between postural balance (CoP) and age and pulmonary function in all patients (table 3).

The occurrence of falls in each group was followed up for 6 months and presented as new fallers or recurrent fallers (figure 5a–c). In the first 3 months of the follow-up period, the highest number of recurrent fallers was observed in the msOSA group, followed by the no OSA and mOSA groups (100%, 80% and 50%, respectively). However, in the 4th–6th follow-up months, every group showed 100% of

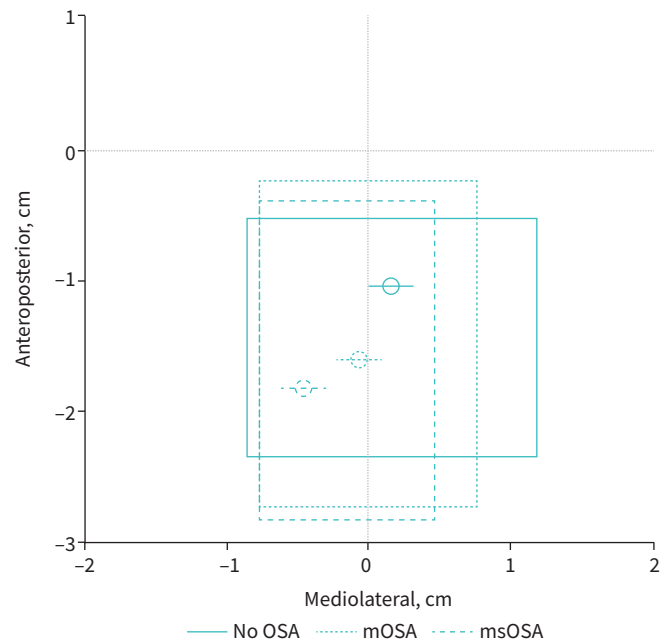


FIGURE 3 The initial centre of pressure of the groups. Circles represent medians and boxes represent interquartile ranges. No OSA: no obstructive sleep apnoea group; mOSA: mild obstructive sleep apnoea group; msOSA: moderate to severe obstructive sleep apnoea group.

recurrent fallers' falls. The effects of some outcomes between fallers and non-fallers were evaluated. However, no between-group difference was observed in the lung function (39.0 (31.0–46.5) % versus 43.0 (37.0–56.0) % of predicted; $p > 0.05$) or in the mean (89.1 (86.0–90.5) % versus 88.8 (86.4–91.0) %; $p > 0.05$) or minimum peripheral oxygen saturation (79.0 (76.0–83.5) % versus 79.0 (74.0–84.0) %; $p > 0.05$). No participant had an exacerbation during the assessment period. One patient with mild OSA was hospitalised due to an exacerbation in the 6-month follow-up, and there was no report of changed medication in this period. Also, two individuals (one in the no OSA group and one in the mild OSA group) began using oxygen during the follow-up.

Discussion

This is the first study to demonstrate that COPD patients with moderate to severe OSA present with alteration in their postural balance, including an increased CoP_{ap} and path length displacements and velocity during postural adjustment. In line with the findings of impaired postural balance, the proportion of recurrent fallers in the follow-up period was higher among patients with moderate to severe OSA than among those without OSA. Additionally, COPD patients with mild OSA presented with intermediate postural balance as compared to those without moderate to severe OSA.

Sleep and postural balance

Comparing our results is difficult due to the lack of similar studies in the literature. DEGACHE *et al.* [21] showed that healthy individuals with sleep disorders (AHI criteria) present postural disturbances, including increased CoP_{ml} and CoP_{ap} displacements. Our results show that only COPD patients with moderate to severe OSA (msOSA group) presented modified CoP; however, they presented an increase in the CoP_{ap} and no difference in CoP_{ml} displacements (figure 4). The msOSA group also presented an increase in postural adjustment, indicating a greater need to keep adjusting the postural balance. The difference between ours and DEGACHE *et al.*'s results could be justified by the fact that our patients were older and had a chronic disease, and the OSA was classified according to severity. Our results seem to contradict those of SMITH *et al.* (2010) [42], who showed that severe COPD patients have a greater mediolateral oscillation but not anteroposterior oscillation. The apparent divergence between our results and those of SMITH *et al.* may be due to two factors. SMITH *et al.* compared the CoP between patients and healthy participants, whereas we did not. Furthermore, they assessed a smaller COPD sample size ($n=12$), while our sample size is six times larger. Additionally, our results are corroborated by those showing that 1 night of sleep deprivation leads to more significant postural oscillation in young adults [43]. If young adults exposed to a single night of sleep deprivation present a change in postural balance, the effect on older

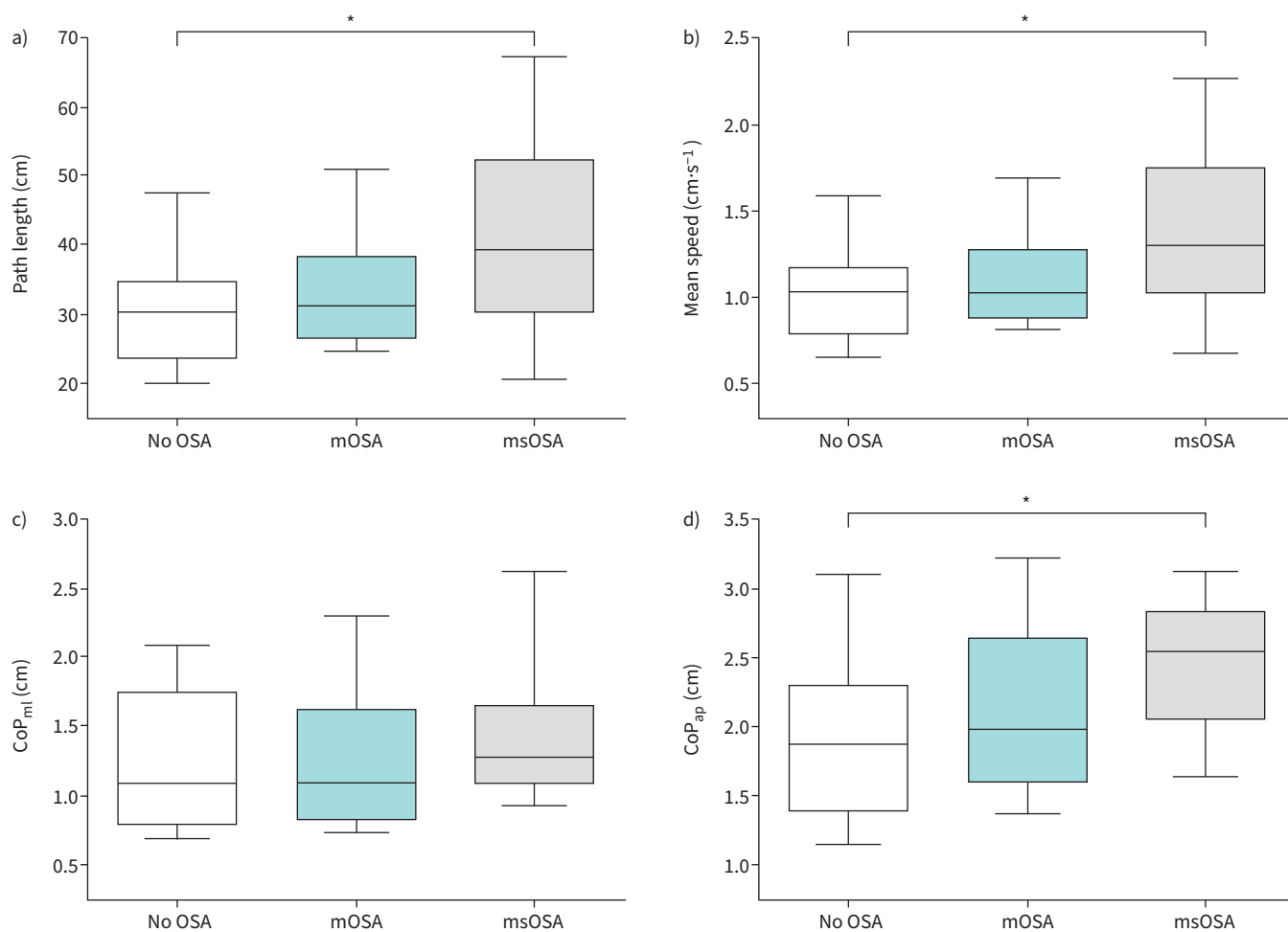


FIGURE 4 The behaviour of the centre of pressure was observed through a) path length, b) mean speed, c) mediolateral displacement and d) anteroposterior displacement. No OSA: no obstructive sleep apnoea group; mOSA: mild obstructive sleep apnoea group; msOSA: moderate to severe obstructive sleep apnoea group; CoP_{ml}: mediolateral centre of pressure; CoP_{ap}: anteroposterior centre of pressure. *: $p < 0.05$ between comparison no OSA and msOSA groups.

individuals with moderate to severe OSA would be even worse. The Mini-BESTest is a validated tool for assessing postural balance in several chronic diseases [33] and is considered effective in predicting falls in patients with COPD [16]. However, the Mini-BESTest scores in our study did not differ between the groups. PEREIRA *et al.* [16] showed that the cut-off value of the Mini-BESTest is 22.5 points for identifying fallers and non-fallers among COPD patients. Since the mean score in all groups in our study was ≥ 23 , above the cut-off value, the Mini-BESTest was probably not sensitive enough to detect a difference in the postural balance induced by OSA.

Sleep disorders, postural balance and age in COPD

The prevalence of OSA in our patients was 57.2%, which is supported by previous studies showing that OSA prevalence ranges from 5 to 85% in patients with COPD [44]. In our study, COPD patients with moderate to severe OSA presented better lung function than those without OSA; however, this difference did not interfere with our comparison, as there was no association between OSA and lung function. Our results are supported by previous findings showing that airway obstruction is not associated with OSA severity in COPD patients [45]. Several risk factors have been associated with OSA, including advanced age, male sex, obesity, cervical and craniofacial circumferences, and upper airway alterations [30, 46]. In our study, COPD patients with moderate or severe OSA were older and had a higher cervical circumference as compared to those of the other groups, which can produce changes in the upper airway and ventilatory control [47]. Moreover, we did not observe an association between postural balance and age, most probably because most patients were elderly (>65 years).

TABLE 3 Linear correlation between postural balance, age, BMI and lung function of all patients

Variable	Age	BMI	FVC	FEV ₁	FEV ₁ /FVC ratio
Path length					
r	0.13	0.02	-0.06	-0.06	-0.09
p	0.26	0.86	0.62	0.57	0.43
Ellipse 95% area					
r	0.21	0.07	-0.11	-0.14	-0.14
p	0.07	0.52	0.35	0.23	0.23
Mean speed					
r	0.14	0.02	-0.05	-0.05	-0.08
p	0.23	0.83	0.65	0.63	0.47
CoP_{ml}					
r	0.27	-0.01	-0.10	-0.15	-0.16
p	0.01*	0.89	0.36	0.20	0.17
CoP_{ap}					
r	0.12	0.17	-0.01	0.06	0.09
p	0.31	0.14	0.92	0.61	0.45

BMI: body mass index; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; CoP_{ml}: mediolateral centre of pressure; CoP_{ap}: anteroposterior centre of pressure; r: Pearson correlation test; p: significance level. *: p<0.05.

Several studies have suggested that COPD patients have impaired balance [11]; however, the underlying mechanisms are not fully understood. In addition, the multisystemic manifestations of COPD seem to be involved in balance deterioration [48–51]. Nevertheless, in the aforementioned study and our study, no correlation was found between balance and pulmonary function when the participants were categorised into disease severity subgroups according to the GOLD criteria. One hypothesis for this finding is that our

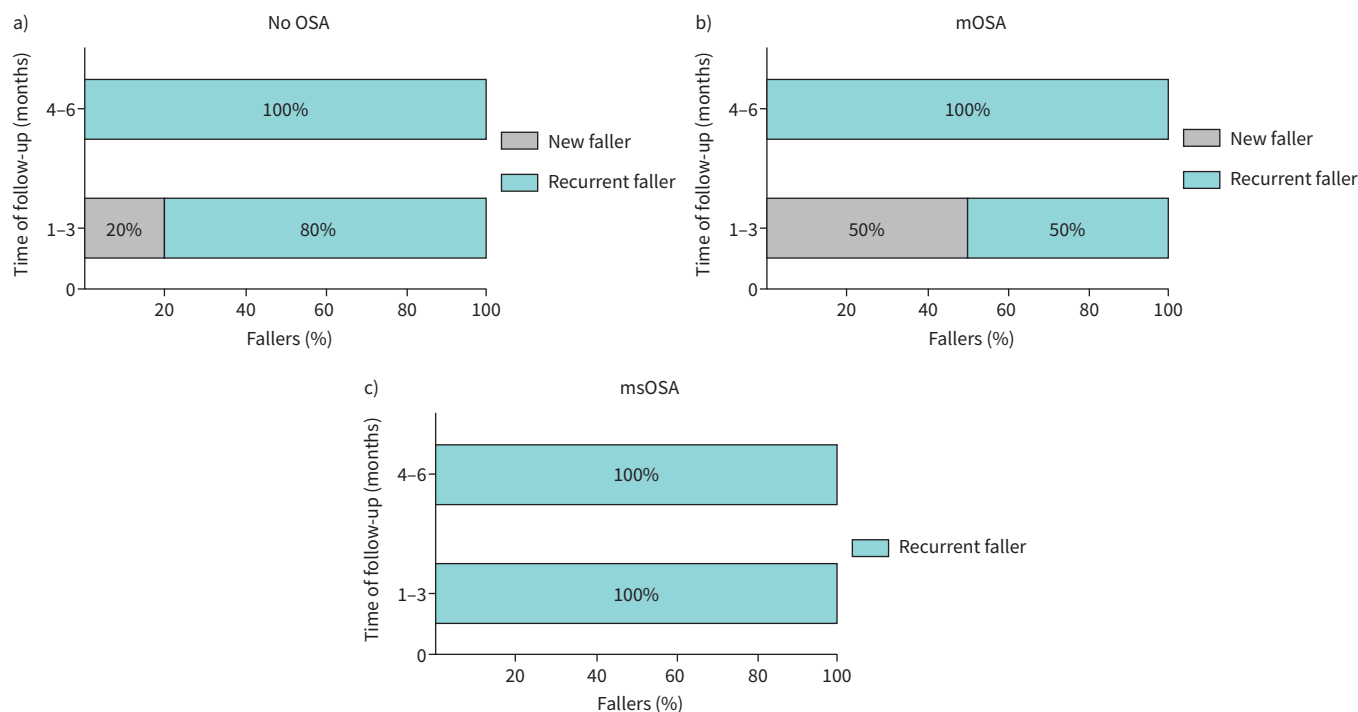


FIGURE 5 The proportion of fallers during 6-month follow-up (n=21). a) No OSA, b) mild OSA and c) moderate to severe OSA. Data are presented for every month of follow-up as the percentage of patients who reported ≥1 fall. A patient was classified as new faller at the first fall report and as a recurrent faller if ≥2 falls occurred within a consecutive 6 months of follow-up. No OSA: no obstructive sleep apnoea group; mOSA: mild obstructive sleep apnoea group; msOAS: moderate to severe obstructive sleep apnoea group.

patients were younger than those who were evaluated in DE CASTRO *et al.*'s [51] study, with a higher degree of sarcopenia [52].

Falls

Our results showing that COPD patients tend to fall repeatedly are supported by those obtained by PEREIRA *et al.* [16]; however, PEREIRA *et al.* did not have OSA subgroups for comparison with our results. Our results showed that 35% of our patients had at least one fall during the 6-month follow-up. These data are supported by studies demonstrating that COPD patients present impaired postural balance and a high risk of falls [12, 13, 42]. Our patients also presented several comorbidities; however, there were no inter-group differences. In addition, we showed that recurrent falls were more common earlier in COPD patients with moderate to severe OSA than in those without OSA in the first trimester, but they were similar at the end of follow-up. Thus, our study has a clinical implication suggesting that patients with moderate and severe OSA require interventions to improve postural balance and reduce the risk of falls; however, this remains to be studied in detail.

Limitations

Our study has some limitations. First, our study included a small sample size that can be considered a bias to the external validation of our findings; however, all the outcomes were assessed using gold standard tools that may reduce possible bias. Second, we excluded oxygen dependency patients because their inclusion could create a bias and impair the comparison of outcomes such as physical activity level. Third, patients with moderate to severe OSA were older and had better lung function than the other groups; however, no association was observed between postural balance and lung function and age. Fourth, our patients did not have a previous record of falls; however, they did not recall falls in the last month before the study. Fifth, patients who performed pulmonary rehabilitation >6 months before the study might have been included, and no previous exercise performance was assessed. Finally, the inclusion criteria included clinical stability and non-exacerbation 4 weeks before the study, but previous use of oral corticosteroids was quantified.

Conclusion

Our results suggest that OSA severity is associated with changes in the postural balance patterns and may increase the risk of recurrent falls in COPD patients. Postural changes include a greater CoP displacement with a more significant anteroposterior oscillation and velocity for the CoP adjustments that worsen with the OSA severity. In contrast, dyspnoea and depression symptoms, quality of life, physical activity levels and mood did not differ between COPD patients with and without OSA.

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Data available on request: The data underlying this article will be shared on reasonable request to the corresponding author.

Conflict of interest: The authors declare that they have no conflicts of interest to disclose.

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