ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Review

Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: A Systematic Review and Meta-Analysis

Rodrigo Núñez-Cortés, Paloma Padilla-Acevedo, Franchesca Vergara-Peña, Sara Mollà-Casanova, Claudia Espinoza-Bravo, Rodrigo Torres-Castro, Carlos Cruz-Montecinos

Please cite this article as: Núñez-Cortés R, Padilla-Acevedo P, Vergara-Peña F, *et al*. Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: A Systematic Review and Meta-Analysis. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00164-2022).

This manuscript has recently been accepted for publication in the *ERJ Open Research*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: A Systematic Review and Meta-Analysis.

Rodrigo Núñez-Cortés[1,2,3,*], Paloma Padilla-Acevedo[1], Franchesca Vergara-Peña[1], Sara Mollà-Casanova[4], Claudia Espinoza-Bravo[5], Rodrigo Torres-Castro[1,3,6], Carlos Cruz-Montecinos[1,2,7]

[1] Departament of Physical Therapy, Faculty of Medicine, University of Chile, Santiago, Chile.

[2] Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), Department of Physiotherapy, University of Valencia

[3] International Physiotherapy Research Network (PhysioEvidence), Barcelona, Spain.

[4] UBIC, Departament de Fisioteràpia, Universitat de València, València, Spain

[5] Day Hospital Unit, Hospital Clínico la Florida, Santiago, Chile.

[6] Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain.

[7] Section of Research, Innovation and Development in Kinesiology, Kinesiology Unit,

San José Hospital, Santiago, Chile.

***Corresponding author:** Rodrigo Núñez-Cortés, Avenida Independencia 1027, Facultad de Medicina, Universidad de Chile, Santiago de Chile.

E-mail: r_nunez@uchile.cl

Abstract

The objective of this study is to compare the balance and functional capacity between stable Chronic Obstructive Pulmonary Disease (COPD) patients versus healthy controls using clinical tests. A comprehensive search of PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and Web of Science was conducted from inception to 21 January 2022. Studies reporting the association between COPD status and balance or functional capacity using clinical tests were included. Two independent reviewers examined the titles and abstracts, extracted the data using a standardised form, and assessed the risk of bias of the included articles. A total of 27 studies with 2,420individuals with stable COPD were included. Overall, the risk of bias in the included studies was low to moderate. The meta-analysis showed a higher history of falls in individuals with COPD (Odds Ratio: 1.59 [95%CI: 1.25-2.02]). Furthermore, an overall effect in favour of the healthy controls was observed in the Timed Up and Go (mean difference: 2.61 seconds [95%CI: 1.79-3.43]), Berg Balance Scale (mean difference: -6.57 points [95%CI: -8.31 to -4.83]), static balance tests (standardized mean difference: -1.36 [95%CI: -2.10 to -0.62]), and the 6-minute walk test (mean difference: -148.21 meters [95%CI: -219.37 to -77.39]). In conclusion, individuals with stable COPD have worse balance and functional capacity compared to healthy controls. These results may guide clinicians to elaborate on therapeutic strategies focused on screening of balance and functional impairments. This is in addition to generating rehabilitation guidelines aimed at reducing the risk of falling in people with COPD.

Keywords: COPD, risk of falls, balance, postural control.

Introduction:

Chronic obstructive pulmonary disease (COPD) is a slowly progressive disease characterised by airflow obstruction mostly affecting the airways and/or lung parenchyma [1]. According to the Global Initiative Obstructive Lung Disease (GOLD), the classification of the severity of airflow limitation is based on the value of the Forced Expiratory Volume in the first second (FEV_1) as a percentage of the predicted value of FEV_1 [2]. The irreversibility and chronicity of the airflow limitation is, therefore, a determining and differential characteristic of other obstructive diseases [3]. COPD is also characterized by persistent symptoms including dyspnea, fatigue, chronic cough, and sputum production or wheezing [4, 5]. Patients with COPD may experience episodes of exacerbations, which involves a sudden worsening of airway function and respiratory symptoms [6]. Although mild episodes of exacerbation are usually reversible, more severe forms of respiratory failure can adversely affect health status and disease prognosis [7]. Stable COPD, on the other hand, is defined as no use of antibiotics, oral corticosteroids or increased use of bronchodilators, and no unscheduled medical visits or hospitalisations due to an acute exacerbation of COPD in the last 4 weeks [8].

The systemic effects of COPD lead to different comorbidities, muscle dysfunction and osteoporosis which in turn lead to inactivity, physical deconditioning, poorer quality of life, and mental health consequences [5, 9, 10]. COPD represents a major public health problem, causing about 3.2 million deaths per year, making it the third leading cause of death worldwide [11]. In addition, due to the global COVID-19 pandemic, COPD patients are currently a population at a higher mortality risk and with greater health care needs [12].

Along with muscle dysfunction and physical deconditioning, people with COPD also have poor balance and a higher incidence of falls compared to people without the disease, even after accounting for factors such as age, gender and others [13]. Falls can have serious health consequences (e.g. hip fractures) and are a major cost to health systems worldwide [14, 15]. Therefore, close monitoring of balance impairment in people with stable COPD is necessary to provide early rehabilitation to reduce the risk of future falls [16]. To assess balance impairment in adults with COPD, different clinical tests have been proposed including static and dynamic balance tests [17]. For example, to assess static balance, the tandem stance or unipodal stance test (UST) are the most commonly used [18]. In the tandem test, subjects were instructed to stand barefoot with the dominant foot just in front of the other [19], while the UST records the time a participant is able to stand on one leg without assistance [18]. Dynamic balance can be assessed using the Timed Up and Go (TUG), which is a timed test of the patient's ability to get up from a chair, walk three metres, turn around and sit back down in the chair [20]. Balance can also be measured by assessing performance on functional tasks using the Berg Balance Scale (BBS) or the Brief Balance Evaluation Systems Test (BESTest) [21]. The BBS measures 14 different performance-based tasks (e.g., rising from a chair, standing on one leg), while the BESTest focuses on 6 different balance control systems: biomechanical constraints, stability limits, anticipatory postural adjustments, postural responses, sensory orientation and gait stability [21]. All these tests show great potential as optimal balance screening tools with high acceptability by clinicians and a short running time [22]. Moreover, in addition to assessing functional capacity, the 6-minute walk test (6MWT) also provides relevant information regarding the fall risk and balance confidence [23].

A previous systematic review collected data throughout March 2019 to quantify the degree of balance impairment in people with COPD compared with healthy controls [24]. While they found that people with COPD have a clinically significant reduction in balance compared to healthy controls, the study population did not specifically focus on stable patients. In addition, no quantitative synthesis was performed to determine whether there was a history of falls or to establish the functional capacity between the two groups. Considering the important differences in balance between individuals with stable COPD and those with an acute exacerbation [24], there is a need to identify the clinical evidence capable of detecting the differences specifically between outpatients with stable COPD and healthy controls. The potential findings may provide a stronger recommendation for fall risk assessments and appropriate balance training in a specific setting (e.g., community-based rehabilitation) [25].

The aim of this study was to synthesise the current evidence and to quantitatively analyse differences in fall risk between outpatients with stable COPD and healthy controls using different clinical tests aimed at assessing balance and fall risk. The secondary objective was to quantitatively assess the differences in the previous history of falls and functional capacity between stable COPD patients and healthy controls.

Methods

This systematic review and meta-analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [26]. The meta-analysis was performed according to the Meta-analysis of Observational Studies in Epidemiology [27]. The protocol was previously registered on the PROSPERO International Prospective Register of Systematic Reviews (number: CRD42020218371) in November 2020.

Eligibility Criteria

The following inclusion criteria were used: 1) randomized controlled trials (RCTs), quasi-randomized clinical trials, and observational studies (cross-sectional, longitudinal, case-control and cohort); 2) studies involving adult participants with a diagnosis of COPD according to international guidelines with a stable pathology; 3) studies involving at least one of the following clinical tests for the assessment of balance and risk of falls in outpatient centres: the BESTest [21], BBS [21], TUG [20], static balance tests with UST, or tandem posture; 4) studies that include an evaluation of physical capacity through clinical tests such as a 6-minute walk test (6MWT) [28], or the sit-to stand test (STS) [29]; 5) studies compared with healthy controls. Studies specifying the inclusion of patients with acute exacerbation of COPD within the last 4 weeks were excluded. Letters to the editor, review articles, systematic reviews, meta-analyses, and in vivo and in vitro studies were excluded.

Search Strategies

A comprehensive search was conducted to identify articles comparing the risk of falls in COPD with respect to healthy controls using different clinical tests. Taking into account the PECO question (population, exposure, comparison, outcome), the following four databases were searched from their inception to January 21, 2022: PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and Web of Science. The following terms were used: 1) For population: adults OR elderly OR older people; 2) For exposure: chronic obstructive pulmonary disease OR COPD; 3) For comparison: healthy subjects OR controls OR healthy pairs; 4) For outcomes: risk of falls OR incidence of falls OR fall rate OR accidental falls OR timed up and go OR TUG OR 6MWT OR walking test OR walk test OR unipedal stance OR chair stand OR STS OR tinetti OR Berg scale OR mini bestest OR bestest. The selected terms were combined using Boolean logical operators (OR, AND, NOT). An additional manual search was performed of the references included in the selected articles and previous systematic reviews.

Selection of the Studies

All articles selected through the database search were exported to the Rayyan software [30], where any duplicates were removed. The review of the articles was performed in two steps. 1) The titles and abstracts of all articles were reviewed and selected by two investigators (FVP, PPA) independently according to the explicit and predefined eligibility criteria. 2) Subsequently, the two reviewers (FVP, PPA) independently reviewed the full-text articles for eligibility. Any discrepancies were resolved by consensus in consultation with a third reviewer (RNC).

Data Extraction

The data extraction was completed independently by each reviewer (PPA, FVP, CEB) following a standardised form. Disagreements were resolved by a third reviewer (RNC). The following variables were collected for each study and entered into a Microsoft Excel (2010) table: author, year of publication, country, study design, number of participants, mean age, sex (%), BMI (kg/m^2), FEV_1, clinical assessment test, outcomes (comparative measure between groups), and conclusion. If any relevant data was not included in the study in the article, the authors were contacted by e-mail to obtain the information.

Bias Risk Assessment

The risk of bias in the included studies was assessed using the Quality in Prognosis Studies (QUIPS) risk of bias tool [31]. This tool includes six dimensions: i) participation, ii) attrition, iii) prognostic factor, iv) outcome measure, v) confounding, vi) analysis and statistical reporting. It classifies the studies into high, moderate and low quality. A low risk of bias was assigned only if the majority (≥75%) of the supporting elements were met, a moderate risk of bias if between 50% and 74% of the supporting elements were satisfied, and a high risk of bias if less than 50% of the elements were met [31]. The quality assessment was evaluated independently by four reviewers (PPA, FVP, SMC, CEB) and a fifth reviewer was consulted to resolve any discrepancies (RNC).

Quantitative Analysis of the Results

The RevMan 5.3 software (The Cochrane Collaboration, Oxford, United Kingdom) was used for the meta-analysis and generation of a forest plot showing the pooled estimates with a 95% confidence interval. To analyse the differences between the participants with COPD and healthy controls in relation to the different variables chosen, random-effects meta-analysis was performed using the mean difference or standardised mean difference (SMD) for a continuous variable or the number of events for a dichotomous variable. If necessary, standard error (SE) was converted into standard deviation (SD). The analysis was performed when four or more studies showed results for the same variable to avoid performing low-power analyses [32]. For this purpose, the results of the studies were grouped according to the variables measured: history of falls, TUG, BBS, static balance test (tandem posture or UST), and 6MWT.

For the heterogeneity analysis, the clinical and methodological differences of the included studies were analysed. For this purpose, the I^2 statistic was used. Following the recommendations of the Cochrane Handbook, we considered that heterogeneity between 0-40% might not be important, while between 30-60% is moderate heterogeneity, between 50%-90% is substantial heterogeneity, and between 75%-100% is considerable heterogeneity [33]. The estimated SMDs were interpreted as follows: SMD of 4.0 to represent an extremely large clinical effect, 2.0-4.0 represented a very large effect, 1.2-2.0 represented a large effect, 0.6-1.2 represented a moderate effect, 0.2-0.6 represented a small effect, and 0.0-0.2 represented a trivial effect [34].

Results

From the search of the databases, 1544 articles were initially identified, leaving 1176 after eliminating duplicates, of which 1126 were excluded during the reading of the title and abstract. The eligibility of the full text of 50 articles was evaluated, excluding 23 studies. Three were excluded due to an erroneous population, seven due to an erroneous design, four due to the type of publication, and the remaining nine due to an erroneous outcome. Finally, a total of 27 articles were included in this systematic review [35–61]. The PRISMA flow chart shows in detail the screening, selection and exclusion process (Figure 1).

Characteristics of the Studies

Table 1 shows the characteristics of the participants in the studies included in this review. All included studies were written in English. Two of them had a prospective design [38, 50], and the remaining twenty-three were cross-sectional studies. A total of 2,420 people with stable COPD were included with an age range of 56.2 ± 4 to 74.9 ± 6.7 years. The FEV_1 of the participants ranged from 27.5% to 59%. Of the included studies, eleven studies used the TUG as a method of assessment in relation to the risk of falls [37, 39, 40, 42, 44, 46–50, 52], nine studies included the BBS as a method of evaluation [35, 37–39, 41, 43, 49, 50, 57], and seven studies included the UST as a method of evaluation [37, 39, 48–50, 52, 56]. Regarding functional capacity, seventeen studies evaluated 6MWT [36, 39, 40, 42, 44, 48–51, 53–55, 57–61]. The narrative synthesis of the results and conclusions of each study is summarized in Table S1 (supplementary material).

Risk of Bias

Figure 2 shows the results of the bias assessment of the articles selected in our review using the QUIPS tool. The bias of all studies was generally classified as "moderate-low bias." Four studies (16%) were "high risk" in one of the QUIPS tool domains: Tudorache et al. 2015 [39] and Porto et al. 2017 [41] in the "confounding" domain, Butcher et al. [52] and Corrêa et al. [54] in the "participations" domain. In contrast, the best evaluated domains were related to the "outcome measurement" and "statistical analysis and reporting" domains, with 96% of the studies classified as "low risk" each, followed by the "prognostic factors" and domain, with 92% of the studies classified as "low risk".

Previous History of Falls

Seven studies collected information regarding the participant's history of previous falls to compare to persons with stable COPD and the healthy controls [35, 38, 39, 41, 43–45]. COPD: 711 participants vs. Control: 569 participants. The overall result of the meta-analysis indicated an increased likelihood in the group of patients with COPD (Odds Ratio: 1.59 [95%CI: 1.25-2.02]) (Figure 3A). The heterogeneity among the studies was low (I^2= 0%).

Time Up and Go (TUG)

Eleven studies used TUG as a measure of balance to compare people with stable COPD with healthy controls [37, 39, 40, 42, 44, 46–50, 52]. COPD: 880 participants vs Control: 412 participants. The overall result of the meta-analysis was in favour of the control group (mean difference: 2.61 seconds [95%CI: 1.79-3.43]) (Figure 3B). The heterogeneity among the studies was considerable (I^2= 93%).

Berg Balance Scale (BBS)

Nine studies used BBS as a measure of balance to compare people with stable COPD with healthy controls [35, 37–39, 41, 43, 49, 50]. COPD: 314 participants vs Control: 199 participants. The overall result of the meta-analysis was favourable towards the control group (mean difference: -6.57 points [95% CI: -8.31 to -4.83]) (Figure 3C). The heterogeneity among the studies was considerable (I^2= 93%).

Static Balance Tests

Seven studies used the UST [37, 39, 49, 50], and one study used the tandem posture [45] as a measure of static balance to compare people with stable COPD with healthy controls. COPD: 515 participants vs Control: 504 participants. The overall result of the meta-analysis was in favour of the control group (standardised mean difference: -1.36 [95%CI: -2.10-0.62]) (Figure 3D). The heterogeneity among the studies was considerable (I^2= 92%).

6-Minute Walk Test (6MWT)

Seventeen studies used the 6MWT as a measure of functional capacity to compare people with stable COPD to healthy controls [36, 39, 40, 42, 44, 48–51, 53–55, 57–61]. COPD: 1226 participants vs Control: 610 participants. The overall result of the meta-analysis was in favour of the control group (mean difference: -148.21 meters [95%CI: -219.37 to -77.39] (Figure 3E). The heterogeneity among the studies was considerable (I^2= 99%).

Discussion

The systematic review and meta-analysis in this study was performed as part of a synthesis of the current evidence to assess the differences in balance and functional capacity between patients with stable COPD and healthy controls using different clinical tests. The results of the qualitative synthesis indicate that subjects with COPD have more history of previous falls and more risk of falling due to worse functional and static balance compared to a control group of healthy subjects. Several clinical tests for functional balance were found to be valid for assessing and predicting the risk of falls in COPD patients with the most commonly used being the TUG and BBS for the dynamic balance assessment, and UST for the static balance assessment. The reduced functional capacity and increased risk of fall is a particularly important point because corticosteroid treatment is often prescribed in the COPD population [2, 62], which may contribute to developing osteopenia or osteoporosis, increasing the risk of hip fracture [63, 64].

Regarding TUG, it has been confirmed as a simple, reliable and useful test to predict the risk of falls and to improve the overall management of people with COPD [65]. The minimum clinically important difference in TUG for COPD patients ranges from 0.9 to 1.4 seconds [66]. Therefore, the differences observed with healthy subjects were above the threshold of clinical relevance defined in the literature (mean difference 2.82 seconds). Among the different causes that could indicate a worse performance in people with COPD, it has been proposed that muscle fatigue together with the increased need for oxygen in the respiratory muscles and the reduction of venous return are the main factors affecting the TUG performance in people with COPD [37].

Regarding BBS, its usefulness at predicting the risk of falls in patients with COPD has been reported and it is recognised as a safe method [39, 41]. Our findings indicated that subjects with COPD had a lower score on the scale, indicating impaired functional balance performance compared to the healthy controls (mean difference -6.57 points). The observed differences in the BBS method exceeded the minimum detectable change reported in the literature of 3.5 points [65].

On the other hand, the included studies also reported that people with COPD have a reduced functional capacity as assessed by the distance covered in the 6MWT. The minimum important difference for the 6MWT in adults with chronic respiratory diseases is between 25 and 33 meters [67]. Therefore, the mean differences observed with the control group of 148 meters exceeded the threshold of clinical relevance. Alterations at the muscular level, mainly of the respiratory and peripheral musculature, are common in COPD patients, leading to fatigue and disability that may increase long-term morbi-mortality [68]. This is while considering that 6MWT is associated with the low performance of both the peripheral musculature and aerobic capacity [69]. In addition, a previous meta-analysis found that shorter 6MWT in COPD patients were correlated with poorer performance on clinical balance outcomes (UST, TUG and BBS) [62]. Future studies could establish whether there is a cut-off threshold to define the risk of falls in this population. In addition, it is important to identify the most vulnerable patients with poorer physical performance and to develop personalised rehabilitation and health promotion strategies [16].

Our systematic review and meta-analysis presents some of the strengths and limitations. Regarding the strengths, a comprehensive search of four databases and additional sources was performed to identify relevant studies that may help clinicians and physiotherapists screen those patients with balance and functional impairments. In addition, most of the included studies were of moderate to high methodological quality. Regarding the limitations, although the meta-analysis showed consistent results, the methodological heterogeneity among the studies was considerable. This could be explained by the fact that although the patients included were all stable, COPD is a disease with different phenotypes, severity, and clinical characteristics. It is likely that the deterioration of balance is also affected by these different conditions. Future studies should include these key aspects to expand the knowledge about the mechanisms related to poor performance in the clinical tests used for assessing balance in COPD patients.

Conclusion

People with stable COPD showed a higher history of falls and have worse static and dynamic balance compared to the healthy controls. Therefore, people with COPD have a higher risk of suffering from a fall compared to subjects without this condition. In addition, people with stable COPD have a lower functional capacity than the healthy controls. These results can guide clinicians to develop therapeutic strategies focused on screening those patients with balance and functional impairments and generating rehabilitation guidelines aimed at reducing the risk of falling in people with COPD.

Funding

S. Mollà-Casanova was supported by the Universitat de València (grant number: INV19-01-13-07). R. Núñez-Cortés was supported by the National Agency for Research and Development (ANID)/Scholarship Program/DOCTORADO BECAS CHILE/2020−72210026. The other authors have nothing to disclose.

Conflict of interest

None

References

1. Celli BR, MacNee W, ATS/ERS Task Force. Standards for the diagnosis and treatment of

patients with COPD: a summary of the ATS/ERS position paper. *Eur. Respir. J.* 2004; 23: 932–946.

2. Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Criner GJ, Frith P, Halpin DMG, Han M, López Varela MV, Martinez F, Montes de Oca M, Papi A, Pavord ID, Roche N, Sin DD, Stockley R, Vestbo J, Wedzicha JA, Vogelmeier C. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *Eur. Respir. J.* [Internet] 2019; 53Available from: http://dx.doi.org/10.1183/13993003.00164-2019.

3. Marín JM. Viejos y nuevos criterios para clasificar la EPOC [Internet]. Archivos de Bronconeumología 2004. p. 9–15Available from: http://dx.doi.org/10.1157/13077907.

4. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Copd: Full Repo 2017. 2016.

5. Ebadi Z, Goërtz YMJ, Van Herck M, Janssen DJA, Spruit MA, Burtin C, Thong MSY, Muris J, Otker J, Looijmans M, Vlasblom C, Bastiaansen J, Prins J, Wouters EFM, Vercoulen JH, Peters JB. The prevalence and related factors of fatigue in patients with COPD: a systematic review. *Eur. Respir. Rev.* [Internet] 2021; 30Available from: http://dx.doi.org/10.1183/16000617.0298-2020.

6. MacIntyre N, Huang YC. Acute exacerbations and respiratory failure in chronic obstructive pulmonary disease. *Proc. Am. Thorac. Soc.* 2008; 5: 530–535.

7. Celli BR, Barnes PJ. Exacerbations of chronic obstructive pulmonary disease. *Eur. Respir. J.* 2007; 29: 1224–1238.

8. Negewo NA, McDonald VM, Baines KJ, Wark PA, Simpson JL, Jones PW, Gibson PG. Peripheral blood eosinophils: a surrogate marker for airway eosinophilia in stable COPD. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2016; 11: 1495–1504.

9. Fiorentino G, Esquinas AM, Annunziata A. Exercise and Chronic Obstructive Pulmonary Disease (COPD). *Adv. Exp. Med. Biol.* 2020; 1228: 355–368.

10. Hakamy A, Bolton CE, McKeever TM. The effect of pulmonary rehabilitation on mortality, balance, and risk of fall in stable patients with chronic obstructive pulmonary disease. *Chron. Respir. Dis.* 2017; 14: 54–62.

11. World Health Organization: WHO. Chronic obstructive pulmonary disease (COPD) [Internet]. World Health Organization: WHO; 2021 [cited 2022 Mar 4].Available from: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd).

12. Ruan Q, Yang K, Wang W, Jiang L, Song J. Correction to: Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China [Internet]. Intensive Care Medicine 2020. p. 1294–1297Available from: http://dx.doi.org/10.1007/s00134-020-06028-z.

13. Hakamy A, Bolton CE, Gibson JE, McKeever TM. Risk of fall in patients with COPD. *Thorax* 2018; 73: 1079–1080.

14. Huang S-W, Wang W-T, Chou L-C, Chen H-C, Liou T-H, Lin H-W. Chronic Obstructive Pulmonary Disease Increases the Risk of Hip Fracture: A Nationwide Population-Based Cohort Study. *Sci. Rep.* 2016; 6: 23360.

15. Falls [Internet]. World Health Organization: WHO; 2021 [cited 2022 Jun 23].Available from: https://www.who.int/news-room/fact-sheets/detail/falls.

16. Canales-Díaz MB, Olivares-Valenzuela C, Ramírez-Arriagada A, Cruz-Montecinos C, Vilaró J, Torres-Castro R, Núñez-Cortés R. Clinical Effects of Rehabilitation on Balance in People With Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *Front. Med.* 2022; 9: 868316.

17. Wang C, Chen H, Qian M, Shi Y, Zhang N, Shang S. Balance Function in Patients With COPD: A Systematic Review of Measurement Properties. *Clin. Nurs. Res.* 2022; : 10547738221078902.

18. Mancini M, Horak FB. The relevance of clinical balance assessment tools to differentiate balance deficits. *Eur. J. Phys. Rehabil. Med.* 2010; 46: 239–248.

19. Franchignoni F, Tesio L, Martino MT, Ricupero C. Reliability of four simple, quantitative tests of balance and mobility in healthy elderly females. *Aging* 1998; 10: 26–31.

20. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Phys. Ther.* 2000; 80: 896–903.

21. Jácome C, Cruz J, Oliveira A, Marques A. Validity, Reliability, and Ability to Identify Fall Status of the Berg Balance Scale, BESTest, Mini-BESTest, and Brief-BESTest in Patients With COPD. *Phys. Ther.* 2016; 96: 1807–1815.

22. McLay R, Kirkwood RN, Kuspinar A, Richardson J, Wald J, Raghavan N, Ellerton C, Pugsley S, Beauchamp MK. Validity of balance and mobility screening tests for

assessing fall risk in COPD. *Chron. Respir. Dis.* 2020; 17: 1479973120922538.

23. Regan E, Middleton A, Stewart JC, Wilcox S, Pearson JL, Fritz S. The six-minute walk test as a fall risk screening tool in community programs for persons with stroke: a cross-sectional analysis. *Top. Stroke Rehabil.* 2020; 27: 118–126.

24. Loughran KJ, Atkinson G, Beauchamp MK, Dixon J, Martin D, Rahim S, Harrison SL. Balance impairment in individuals with COPD: a systematic review with meta-analysis. *Thorax* 2020; 75: 539–546.

25. Xia QH, Jiang Y, Niu CJ, Tang CX, Xia ZL. Effectiveness of a community-based multifaceted fall-prevention intervention in active and independent older Chinese adults. *Inj. Prev.* 2009; 15: 248–251.

26. Moher D. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement [Internet]. Annals of Internal Medicine 2009. p. 264Available from: http://dx.doi.org/10.7326/0003-4819-151-4-200908180-00135.

27. Stroup DF. Meta-analysis of Observational Studies in EpidemiologyA Proposal for Reporting [Internet]. JAMA 2000. p. 2008Available from: http://dx.doi.org/10.1001/jama.283.15.2008.

28. Mănescu V. [The relevance of the 6 minutes walking test and of dyspnea measured with mMRC scale in evaluating COPD severity]. *Pneumologia* 2012; 61: 153–159.

29. Vaidya T, Chambellan A, de Bisschop C. Sit-to-stand tests for COPD: A literature review. *Respir. Med.* 2017; 128: 70–77.

30. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app

for systematic reviews. *Syst. Rev.* 2016; 5: 210.

31. Grooten WJA, Tseli E, Äng BO, Boersma K, Stålnacke B-M, Gerdle B, Enthoven P. Elaborating on the assessment of the risk of bias in prognostic studies in pain rehabilitation using QUIPS-aspects of interrater agreement. *Diagn Progn Res* 2019; 3: 5.

32. Jackson D, Turner R. Power analysis for random-effects meta-analysis. *Res Synth Methods* 2017; 8: 290–302.

33. Higgins JPT, Thomas J. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons; 2019.

34. Hopkins WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies in sports medicine and exercise science. *Med. Sci. Sports Exerc.* 2009; 41: 3–13.

35. Beauchamp MK, Sibley KM, Lakhani B, Romano J, Mathur S, Goldstein RS, Brooks D. Impairments in systems underlying control of balance in COPD. *Chest* 2012; 141: 1496–1503.

36. Iwakura M, Okura K, Shibata K, Kawagoshi A, Sugawara K, Takahashi H, Shioya T, Wakasa M. Gait characteristics and their associations with clinical outcomes in patients with chronic obstructive pulmonary disease. *Gait Posture* 2019; 74: 60–65.

37. Crişan AF, Oancea C, Timar B, Fira-Mladinescu O, Tudorache V. Balance impairment in patients with COPD. *PLoS One* 2015; 10: e0120573.

38. Oliveira CC, Lee AL, McGinley J, Anderson GP, Clark RA, Thompson M, Clarke S, Baker T, Irving LB, Denehy L. Balance and Falls in Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Prospective Study. *COPD* 2017; 14: 518–525.

39. Tudorache E, Oancea C, Avram C, Fira-Mladinescu O, Petrescu L, Timar B. Balance impairment and systemic inflammation in chronic obstructive pulmonary disease. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2015; 10: 1847–1852.

40. Albarrati AM, Gale NS, Enright S, Munnery MM, Cockcroft JR, Shale DJ. A simple and rapid test of physical performance inchronic obstructive pulmonary disease. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2016; 11: 1785–1791.

41. Porto EF, Pradella CO, Rocco CM, Chueiro M Jr, Maia RQ, Ganança FF, Castro AAM, Nascimento OA, Jardim JR. Comparative Postural Control in COPD Patients and Healthy Individuals During Dynamic and Static Activities. *J. Cardiopulm. Rehabil. Prev.* 2017; 37: 139–145.

42. de Castro LA, Ribeiro LR, Mesquita R, de Carvalho DR, Felcar JM, Merli MF, Fernandes KB, da Silva RA, Teixeira DC, Spruit MA, Pitta F, Probst VS. Static and Functional Balance in Individuals With COPD: Comparison With Healthy Controls and Differences According to Sex and Disease Severity. *Respir. Care* 2016; 61: 1488–1496.

43. Oliveira CC, McGinley J, Lee AL, Irving LB, Denehy L. Fear of falling in people with chronic obstructive pulmonary disease. *Respir. Med.* 2015; 109: 483–489.

44. Al Haddad MA, John M, Hussain S, Bolton CE. Role of the Timed Up and Go Test in Patients With Chronic Obstructive Pulmonary Disease. *J. Cardiopulm. Rehabil. Prev.* 2016; 36: 49–55.

45. Gore S, Blackwood J, Ziccardi T. Associations Between Cognitive Function, Balance, and Gait Speed in Community-Dwelling Older Adults with COPD. *J. Geriatr. Phys. Ther.*

[Internet] 2021; Available from: http://dx.doi.org/10.1519/JPT.0000000000000323.

46. Jirange P, Vaishali K, Sinha MK, Bairapareddy KC, Alaparthi GK. A Cross-Sectional Study on Balance Deficits and Gait Deviations in COPD Patients. *Can. Respir. J.* 2021; 2021: 6675088.

47. Ozsoy I, Ozsoy G, Kararti C, Buyukturan B, Yilmaz F, Buyukturan O, Erturk A. Cognitive and motor performances in dual task in patients with chronic obstructive pulmonary disease: a comparative study. *Ir. J. Med. Sci.* 2021; 190: 723–730.

48. Schons P, da Silva ES, Coertjens M, Oliveira HB, Fischer G, Costa RR, Preissler AAB, Knorst MM, Peyré-Tartaruga LA. The relationship between height of vertical jumps, functionality and fall episodes in patients with chronic obstructive pulmonary disease: A case-control study. *Exp. Gerontol.* 2021; 152: 111457.

49. Voica AS, Oancea C, Tudorache E, Crisan AF, Fira-Mladinescu O, Tudorache V, Timar B. Chronic obstructive pulmonary disease phenotypes and balance impairment. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2016; 11: 919–925.

50. Mkacher W. Changes in balance after rehabilitation program in patients with COPD and in healthy subjects. *Int. J. Phys. Med. Rehabil.* [Internet] OMICS Publishing Group; 2014; 02Available from: https://www.omicsonline.org/open-access/changes-in-balance-after-rehabilitation-program-in-patients-with-copd-and-in-healthy-subjects-2329-9096.1000219.php?aid=28554.

51. Amorim PB, Stelmach R, Carvalho CRF, Fernandes FLA, Carvalho-Pinto RM, Cukier A. Barriers associated with reduced physical activity in COPD patients. *J. Bras. Pneumol.*

2014; 40: 504–512.

52. Butcher SJ, Meshke JM, Sheppard MS. Reductions in functional balance, coordination, and mobility measures among patients with stable chronic obstructive pulmonary disease. *J. Cardiopulm. Rehabil.* 2004; 24: 274–280.

53. Chien J-Y, Ruan S-Y, Huang Y-CT, Yu C-J, Yang P-C. Asynchronous thoraco-abdominal motion contributes to decreased 6-minute walk test in patients with COPD. *Respir. Care* 2013; 58: 320–326.

54. Corrêa KS, Karloh M, Martins LQ, dos Santos K, Mayer AF. Can the Glittre ADL test differentiate the functional capacity of COPD patients from that of healthy subjects? *Rev. Bras. Fisioter.* 2011; 15: 467–473.

55. Hernandes NA, Teixeira D de C, Probst VS, Brunetto AF, Ramos EMC, Pitta F. Profile of the level of physical activity in the daily lives of patients with COPD in Brazil. *J. Bras. Pneumol.* 2009; 35: 949–956.

56. Iwakura M, Okura K, Shibata K, Kawagoshi A, Sugawara K, Takahashi H, Shioya T. Relationship between balance and physical activity measured by an activity monitor in elderly COPD patients [Internet]. International Journal of Chronic Obstructive Pulmonary Disease 2016. p. 1505–1514Available from: http://dx.doi.org/10.2147/copd.s107936.

57. Ozalevli S, Ilgin D, Narin S, Akkoclu A. Association between disease-related factors and balance and falls among the elderly with COPD: a cross-sectional study. *Aging Clin. Exp. Res.* 2011; 23: 372–377.

58. Roig M, Eng JJ, MacIntyre DL, Road JD, Reid WD. Deficits in muscle strength, mass, quality, and mobility in people with chronic obstructive pulmonary disease. *J. Cardiopulm. Rehabil. Prev.* 2011; 31: 120–124.

59. Serrão NF Jr, Porta A, Minatel V, Castro AAM, Catai AM, Sampaio LMM, Arena R, Borghi-Silva A. Complexity analysis of heart rate variability in chronic obstructive pulmonary disease: relationship with severity and symptoms. *Clin. Auton. Res.* 2020; 30: 157–164.

60. Ilgin D, Ozalevli S, Kilinc O, Sevinc C, Cimrin AH, Ucan ES. Gait speed as a functional capacity indicator in patients with chronic obstructive pulmonary disease. *Ann. Thorac. Med.* 2011; 6: 141–146.

61. Annegarn J, Spruit MA, Savelberg HHCM, Willems PJB, van de Bool C, Schols AMWJ, Wouters EFM, Meijer K. Differences in walking pattern during 6-min walk test between patients with COPD and healthy subjects. *PLoS One* 2012; 7: e37329.

62. Loughran KJ, Atkinson G, Beauchamp MK, Dixon J, Martin D, Rahim S, Harrison SL. P125 Balance impairment and clinical associations in individuals with COPD: a systematic review with meta-analysis [Internet]. COPD: clinical investigation 2018.Available from: http://dx.doi.org/10.1136/thorax-2018-212555.283.

63. Lehouck A, Boonen S, Decramer M, Janssens W. COPD, bone metabolism, and osteoporosis. *Chest* 2011; 139: 648–657.

64. Sutter SA, Stein EM. The Skeletal Effects of Inhaled Glucocorticoids. *Curr. Osteoporos. Rep.* 2016; 14: 106–113.

65. Mkacher W, Tabka Z, Trabelsi Y. Minimal Detectable Change for Balance Measurements in Patients With COPD. *J. Cardiopulm. Rehabil. Prev.* 2017; 37: 223–228.

66. Mesquita R, Wilke S, Smid DE, Janssen DJ, Franssen FM, Probst VS, Wouters EF, Muris JW, Pitta F, Spruit MA. Measurement properties of the Timed Up & Go test in patients with COPD. *Chron. Respir. Dis.* 2016; 13: 344–352.

67. Singh SJ, Puhan MA, Andrianopoulos V, Hernandes NA, Mitchell KE, Hill CJ, Lee AL, Camillo CA, Troosters T, Spruit MA, Carlin BW, Wanger J, Pepin V, Saey D, Pitta F, Kaminsky DA, McCormack MC, MacIntyre N, Culver BH, Sciurba FC, Revill SM, Delafosse V, Holland AE. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *Eur. Respir. J.* 2014; 44: 1447–1478.

68. Maltais F, Leblanc P, Jobin J, Casaburi R. [Peripheral muscle dysfunction in chronic obstructive pulmonary disease]. *Rev. Mal. Respir.* 2002; 19: 444–453.

69. Cruz-Montecinos C, Guajardo-Rojas C, Montt E, Contreras-Briceño F, Torres-Castro R, Díaz O, Cuesta-Vargas A. Sonographic Measurement of the Quadriceps Muscle in Patients With Chronic Obstructive Pulmonary Disease: Functional and Clinical Implications. *J. Ultrasound Med.* 2016; 35: 2405–2412.

Table 1. Characteristics of the included studies.

Study, years (country)	Study design	n (M/F)	Age (years)	BMI (kg/m₂)	FEV_1 (% Predicted)	Outcome
Butcher et.al, 2004 (Canada)	Cross-sectional	COPD (NO): 15 (7/8) COPD (WO): 15 (5/10) Control: 21 (3/18)	COPD (NO): 72±2 COPD (WO): 69±2 Control: 68±1	NR	COPD (NO): 45±3 COPD (WO): 29±3 Control: 105 ± 3	TUG
Hernandes et al, 2009 (Brazil)	Cross-sectional	COPD: 40 (18/22) Control: 30 (14/6)	COPD: 66±8 Control: 64±7	COPD: 27±6 Control: 28±4	COPD: 46±16 Control: 111±20	6MWT
Ozalevli et al. 2010 (Turkey)	Cross-sectional	COPD: 36 (25/11) Control: 20 (13/7)	COPD: 70.3±3 Control: 68.5±7.3	COPD: 24.6±5 Control: 27.6 ± 2.6	COPD: 43.5±6 Control: 98.3±11.1	BBS, 6MWT
Corrêa et.al 2011 (Brazil)	Cross-sectional	COPD: 10 (3/7) Control: 10 (3/7)	COPD: 64±10 Control: 63±7	COPD: 23±5 Control: 24±3	COPD: 38±11 Control: 95±18	6MWT
Roig et al. 2011 (Canada)	Cross-sectional	COPD: 21 (NR/NR) Control: 21 (NR/NR)	COPD: 71.2±8.1 Control: 67.4±7.6	COPD: 25.6±4.2 Control: 25.3±4	COPD: 47.2±12.9 Control: 98.1±11.9	6MWT
Ilgin et al. 2011 (Turkey)	Cross-sectional	COPD: 511 (NR/NR) Control: 113 (NR/NR)	GOLD I: 63.7±10.6 GOLD II: 67.1±9.5 GOLD III 66.0±9.8 GOLD IV 62.7±8.6 Control: 61.7±9.9	GOLD I: 25.7±3.8 GOLD II: 25.6±3.9 GOLD III: 25.4±4.6 GOLD IV 25.3±5.0 Control: 27.2±4.2	GOLD I: 90.0±8.4 GOLD II: 64.0±8.3 GOLD III 39.5±5.8 GOLD IV: 25.0±3.2 Control: 99.3±16.9	6MWT
Beauchamp et al. 2012 (Canada)	Cross-sectional	COPD: 37 (17/20) Control: 20 (8/12)	COPD: 71±7 Control: 67±9	COPD: 28.9±10.5 Control: 24.8±3.4	COPD: 39.4±16.3 Control: 96.9±15.9	BESTest, BBS, ABC
Annegarn et al. 2012	Cross-	COPD: 79 (47/32)	COPD: 64.3±8.9	COPD: 24.7±4.5	COPD: 53.5±18.7	6MWT

(Netherlands)	sectional	Control: 24 (15/9)	Control: 63.7±5.9	Control: 25.8±3.8	Control:124.9±21.0	
Chien et al. 2013 (China)	Cross-sectional	Moderate COPD: 40 (37/7) Severe COPD: 48 (30/10). Control: 14 (12/2)	COPD: moderate/severe 67±1 / 69±1 Control: 62±2	Moderate COPD: 24.3±0.6 Severe COPD: 22.2±0.6 Control: 23±1	Moderate COPD: 67±1 Severe COPD: 35±1 Control: 92±2	6MWT
Amorin et. al. 2014 (Brazil)	Cross-sectional	COPD: 40 (22/18) Control: 20(19/21)	COPD: 64±7 Control: 66±10	COPD: 25 ± 3 Control: 25 ± 3	COPD: 47 ± 15 Control: 109 ± 13	6MWT
Mkacher et al. 2014 (Tunisia)	Prospective	COPD: 16 (16/0) Control: 18 (18/0)	COPD: 56.22±4.12 Control 58.06±2.91	COPD: 26,47±1,78 Control 26,16±1,59	COPD: 49.75±2,56 Control 90,27±5,76	TUG, SLS, BBS
Crisan et al. 2015 (Romania)	Cross-sectional	COPD: 29 (NR/NR) Control: 17 (NR/NR)	COPD: 62.2±5.0 Control: 61.4±4.0	COPD: 25.4±3.6 Control: 25.3±3.9	COPD: 29±7 Control: 95±18	BBS, SLS, TUG
Oliveira et al. 2015 (Australia)	Cross-sectional	COPD: 40 (19/21) Control: 25 (12/13)	COPD: 71±8 Control: 69±8	COPD: 25.0±4.8 Control: 24.6±3.4	COPD: 45.1±16.2 Control:102.1±12.8	FOF, FES-I, BBS, 6MWT
Tudorache et al. 2015 (Rumania)	Cross-sectional	COPD: 22 (NR/NR) Control: 20 (NR/NR)	COPD: 63 ± 5 Control: 63 ± 4	COPD: 24.2 ± 5.7 Control: 24.9 ± 3.8	COPD: 27.5 (7%) Control: 100.5 (12%)	FES-I, BBS, TUG, SLS, 6MWT
Iwakura et al. 2016 (Japan)	Cross-sectional	COPD: 22 (H) Control: 13 (H)	COPD: 71.6 ± 6.9 Control: 71.5 ± 5.6	COPD: 22.1 ± 2.9 Control: 22.7 ± 2.5	COPD: 52.8 ± 20.6 Control: 94.7 ± 26.7	SLS, 6MWT
Voica et al. 2016 (Romania)	Cross-sectional	COPD: 27 (NR/NR) Control: 17 (NR/NR	Emphysematous COPD: 64.1±2.6 Bronchitic COPD: 63.9±1.9 Control: 61.3±4.0	Emphysematous COPD: 17.6±0.8 Bronchitic COPD: 36.1±3.3 Control: 25.3±3.9	Emphysematous COPD: 31 ± 2 Bronchitic COPD: 30 ± 4 Control: 95 ± 18	TUG, SLS, BBS, 6MWT
Albarrati et al. 2016 (United Kingdom)	Cross-sectional	COPD: 520 (270/250) Control: 150 (76/74)	COPD: 66.1 ± 7.6 Control: 65 ± 7.4	COPD: 28.0±5.5 Control: 28.1±4.1	COPD: 58 ± 19 Control: 105 ± 14	6MWT, TUG

Alhaddad et al. 2016 (United Kingdom)	Cross-sectional	COPD: 119 (74/45) Control: 58 (38/20)	COPD: 68 ± 8 Control: 66 ± 9	COPD: 27.3 ± 6 Control: 28.6 ± 5.2	COPD: 59 ± 18 Control: 100 ± 15	TUG, 6MWT
Decastro et al. 2016 (Brazil)	Cross-sectional	COPD: 47 (27/20) Control: 25(15/10)	COPD: 68 ± 5 Control: 66 ± 8	COPD: 26 ± 5 Control: 28 ± 5	COPD: 45 ± 15 Control: 87 ± 17	TUG, 6MWT
Oliveira et al. 2017 (Australia)	Prospective	COPD: 26 (13/13) Control: 25 (12/13)	COPD: 70 ± 9 Control: 70 ± 8	COPD: 25 ± 7 Control: 24 ± 3	COPD: 44 ± 18 Control: 102 ± 12	BBS
Porto et al. 2017 (Brazil)	Cross-sectional	COPD: 93 (61%/39%) Control: 39 (41%/59%)	COPD: 67.3 ± 10.8 Control: 65.1 ± 9.7	NR	COPD: 50.4 ± 19 Control: 89.2 ± 23.6	BBS, FES-I
Iwakura et al. 2019 (Japan)	Cross-sectional	COPD: 34 (34/0) Control: 16 (16/0)	COPD: 71 ± 8 Control: 72 ± 6	COPD: 21.8 ± 2.8 Control: 22.8 ± 2.3	COPD: 57± 28 Control:102 ± 19	6MWT
Serrão et.al, 2020 (Brazil)	Cross-sectional	COPD: 54 (43/10) Control: 20 (17/3)	COPD: 66 ± 8 Control: 65 ± 8	COPD: 24 ± 4 Control: 25 ± 3	COPD: 34 ± 9 Control: 101 ± 16	6MWT
Gore et al.2021 (Estados Unidos)	Cross-sectional	COPD: 382 (43.5%/56.5%) Control: 382 (41.5%/58.4%)	COPD: 74.94 ± 6.75 Control: 75.23 ± 6.92	COPD: 29.94 ± 6.69 Control: 30.39 ± 5.34	NR	Tandem posture
Jirange et al. 2021 (India)	Cross-sectional	COPD: 42 Control: 45	COPD: 61.9 ± 4.61 Control: 60.47 ± 6.18	COPD: 22.22 ± 3.31 Control: 23.50 ± 3.27	COPD: 37.3±7.99 Control: NR	TUG
Ozsoy et al. 2021 (Turkey)	Cross-sectional	COPD: 35 (89.2%/10.8%) Control: 27 (84%/16%)	COPD: 62.13 ± 8.17 Control: 60.60 ± 7.84	COPD: 27.95 ± 4.72 Control: 29.07 ± 3.25	COPD: 59.18 ± 15.32 Control: NR	TUG
Schons et al. 2021 (Brazil)	Case-control study	COPD: 20 (9/11) Control: 16 (7/9)	COPD: 62.95 ± 8.06 Control: 59.94 ± 6.43	COPD: 68.80 ± 14.92 Control: 68.06 ± 16.11	COPD: 39.98 ± 11.69% Control: 97.44 ± 14.45%	6MWT, SLS, TUG

Abbreviations: 6MWT, 6-minute walk test; ABC, Activity-specific balance of confidence scale; BMI, body mass index; COPD, chronic obstructive pulmonary disease; BBS, Berg Balance Scale; BESTest, Balance Evaluation Systems Test; FOF, Fear of Falling; F, female; FEV_1, Forced expiratory volume in the first second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; M, male; NR, not reported; TUG, Timed Up and Go; SLS, single leg stance.

Figure 1. Study selection process

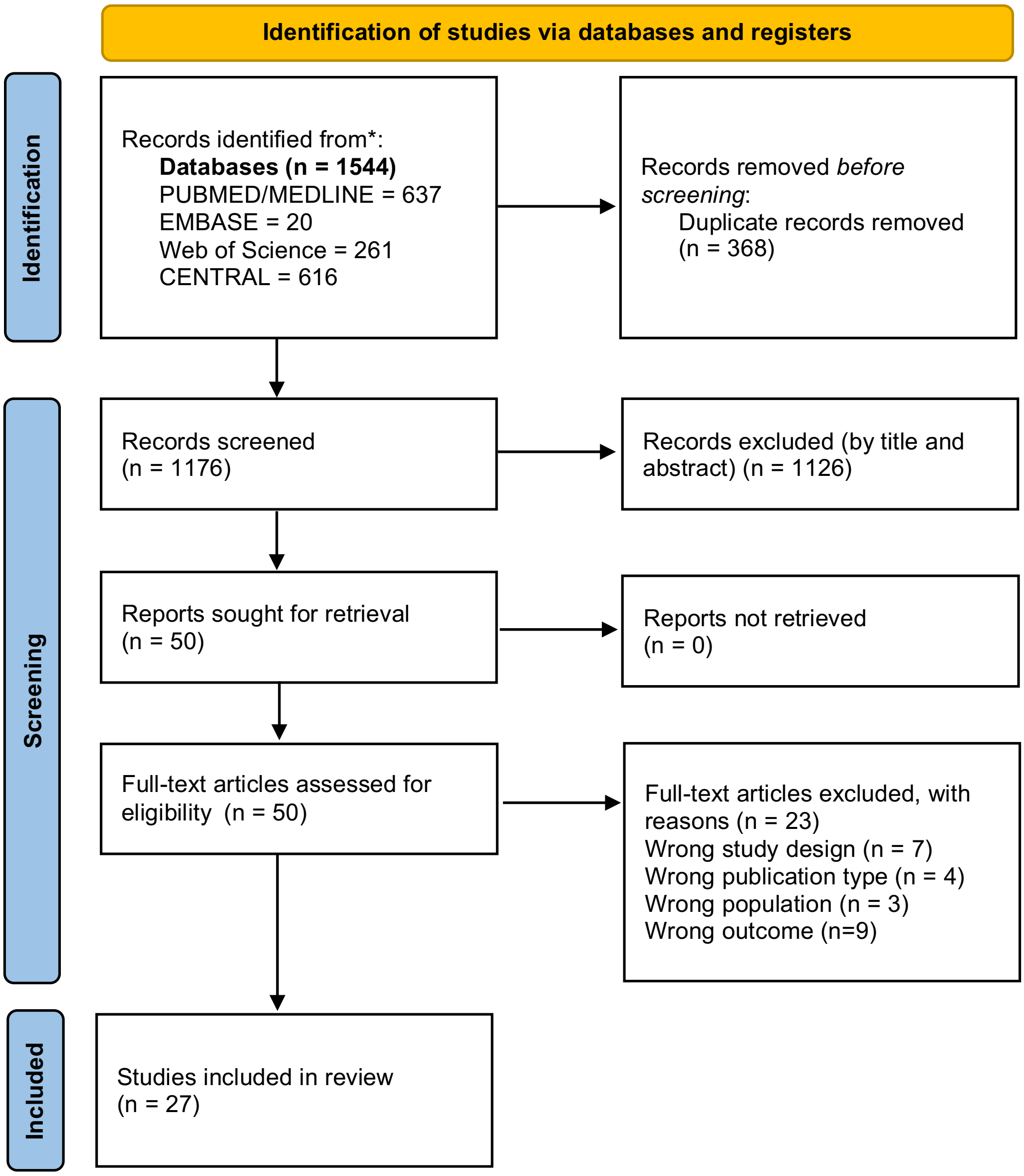


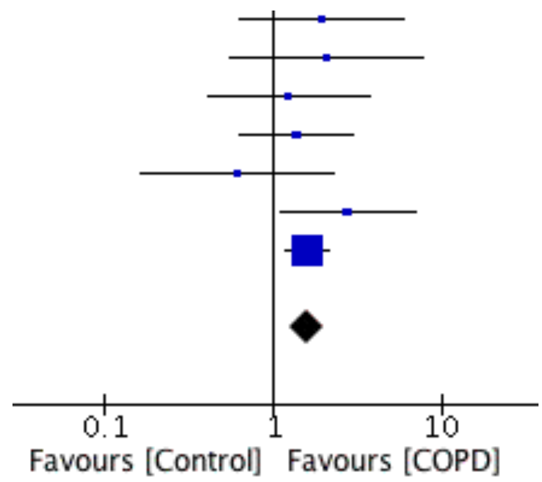
Figure 2. Summary of risk of bias assessment using the QUIPS tool.

Figure 3. Quantitative Synthesis.

A **Previous History of Falls**

Study	Weight	OR (95% CI)
Beauchamp 2012	4.6%	1.96 [0.64, 6.02]
Tudorache 2015	3.3%	2.08 [0.55, 7.79]
Oliveira 2015	4.8%	1.24 [0.41, 3.70]
Al Haddad 2016	9.3%	1.37 [0.63, 3.02]
Oliveira 2017	3.4%	0.61 [0.17, 2.27]
Porto 2017	6.8%	2.76 [1.10, 6.92]
Gore 2021	67.7%	1.59 [1.19, 2.13]
Total (95% CI)	**100.0%**	**1.59 [1.25, 2.02]**

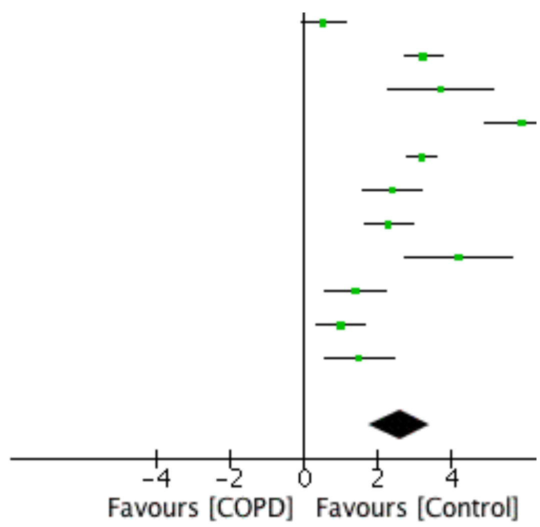
Heterogeneity: I^2=0%, Chi^2 = 4.05 (P=0.67)



B **Timed Up and Go**

Study	Weight	MD (95% CI)
Butcher 2004	9.6%	0.52 [-0.08, 1.12]
Mkacher 2014	9.7%	3.23 [2.71, 3.75]
Crisan 2015	7.8%	3.70 [2.29, 5.11]
Tudorache 2015	8.7%	5.90 [4.87, 6.93]
Albarrati 2016	9.9%	3.20 [2.81, 3.59]
Al Haddad 2016	9.2%	2.40 [1.59, 3.21]
Decastro 2016	9.6%	2.30 [1.66, 2.94]
Voica 2016	7.7%	4.20 [2.76, 5.64]
Schons 2021	9.2%	1.40 [0.58, 2.22]
Jirange 2021	9.6%	1.00 [0.37, 1.63]
Ozsoy 2021	8.9%	1.50 [0.55, 2.45]
Total (95% CI)	**100.0%**	**2.61 [1.79, 3.43]**

Heterogeneity: I^2=93%, Chi^2 = 145.39 (P<0.001)



C **Berg Balance Scale**

Study	Weight	MD (95% CI)
Ozalevli 2010	9.2%	-19.20 [-22.31, -16.09]
Beauchamp 2012	11.1%	-6.20 [-8.20, -4.20]
Mkacher 2014	12.3%	-5.14 [-6.21, -4.07]
Crisan 2015	9.8%	-2.00 [-4.72, 0.72]
Oliveira 2015	11.9%	-3.60 [-5.01, -2.19]
Tudorache 2015	10.2%	-7.00 [-9.52, -4.48]
Voica 2016	11.2%	-10.00 [-11.89, -8.11]
Oliveira 2017	11.4%	-3.50 [-5.28, -1.72]
Porto 2017	12.9%	-4.90 [-5.11, -4.69]
Total (95% CI)	**100.0%**	**-6.57 [-8.31, -4.83]**

Heterogeneity: I^2=93%, Chi^2 = 122.84 (P<0.001)

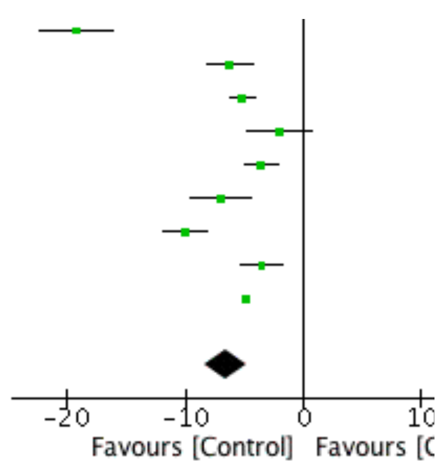
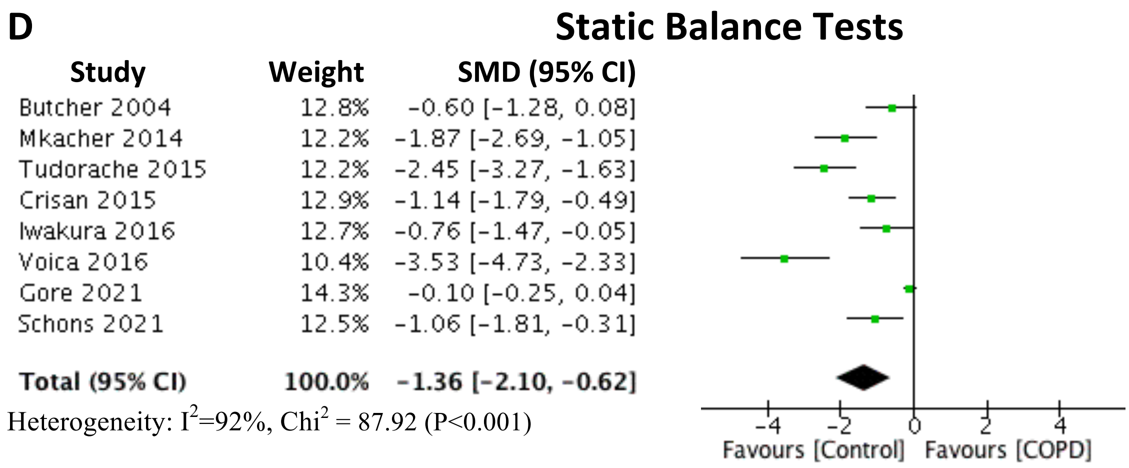
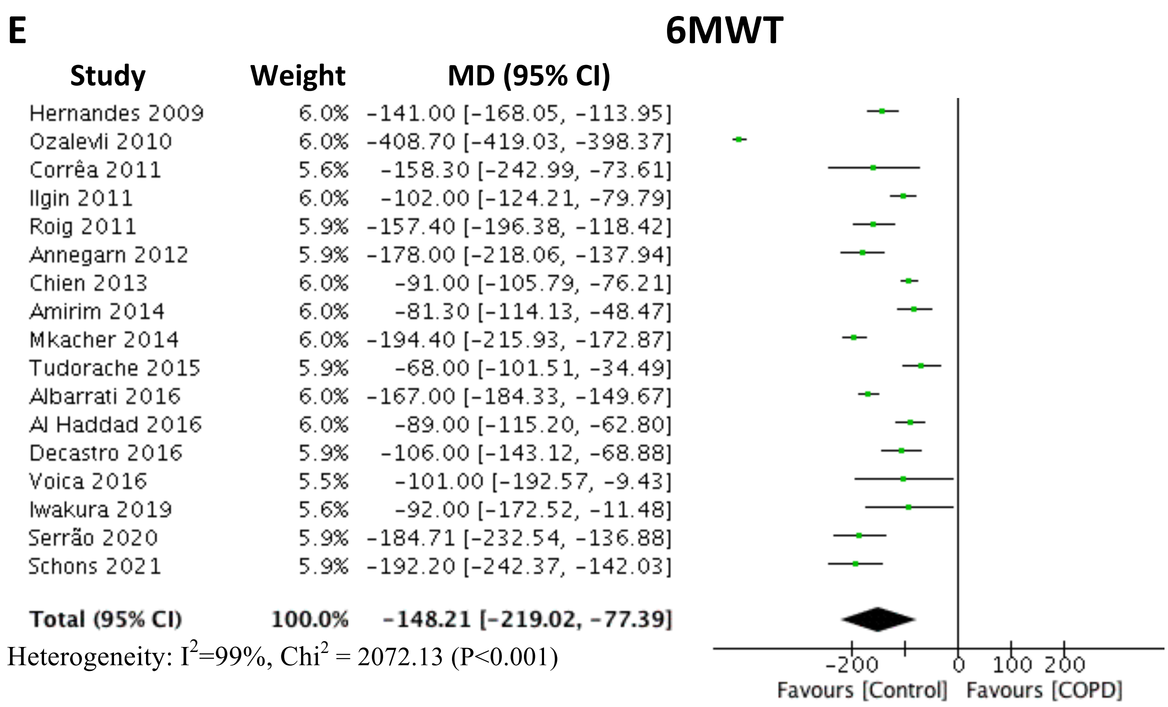


Figure 3. Continued





Abbreviations: 6MWT, 6-minute walk test; 95%CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; MD, Mean Difference; OR, Odds Ratio; SMD, Std. Mean Difference.

A) Forest plot of the comparison of history of previous falls between people with COPD and healthy controls; B) Forest plot of the comparison of TUG between people with COPD and healthy controls; C) Forest plot of the comparison of BBS between people with COPD and healthy controls; D) Forest plot of the comparison of balance static tests between people with COPD and healthy control; E) Forest plot of the comparison of 6MWT between people with COPD and healthy controls. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the graph corresponds to the summary effect, and its width represents its 95% CI.

S1. Summary of results

Study, years	n	Results	Conclusion
Butcher et.al, 2004	COPD: 15 Control: 21	Significant differences in TUG were observed when oxygen-dependent COPD patients were compared against the COPD without oxygen and healthy controls groups. (COPD with oxygen: 7.2 ± 0.4 v/s COPD without oxygen: 5.8 ± 0.4, Control: 5.3 ± 0.3).	Significant differences in balance were observed when comparing controls and non-oxygen-dependent COPD with oxygen-dependent COPD. There were no differences when comparing healthy controls with the non-oxygen-dependent COPD group.
Hernandes et al, 2009	COPD: 40 Control: 30	Statistically significant differences were observed in COPD patients on the 6MWT relative to controls. (COPD: 419 ± 111 v/s Control: 560 ± 75).	COPD patients had lower exercise capacity than healthy controls.
Ozalevli et al. 2010	COPD: 36 Control: 20	BBS scores were significantly different between COPD patients and healthy individuals (p=0.001). The 6MWT of COPD patients was shorter than that of healthy individuals (111.5±12.0 vs. 520.2±21.8, p=0.001).	The findings suggest that assessment and training to improve balance impairment among the elderly with COPD should be a component of pulmonary rehabilitation programs in clinical practice.
Correa et.al 2011	COPD: 10 Control: 10	Statistically significant differences were observed in COPD patients on the 6MWT relative to controls. (COPD: 434 ± 105 v/s Control: 593 ± 87).	COPD patients had lower exercise capacity than healthy controls.
Roig et a. 2011	COPD: 21 Control: 21	Statistically significant differences were observed in individuals with COPD on 6MWT relative to controls. (<0.001).	Compared with healthy controls, people with moderate to severe COPD show marked deficits in mobility.
Ilgin et al. 2011	COPD: 511 Control: 113	Statistically significant differences were observed in COPD patients on 6MWT relative to controls. (COPD: 397.5 ± 63.9v/s Control: 554.9 ± 65).	Walking distance and walking speed decrease with increasing COPD severity
Beauchamp et al. 2012	COPD: 37 Control: 20	COPD subjects demonstrated lower balance on each component of the total BESTest (70.7% ±11.3), with marked deficits, compared to controls (91.9% ±4.0); differences were also observed on the BBS (48.7±5.7 points) compared to healthy subjects (54.9±1.8 points).	COPD patients show reductions in subcomponents of postural control, shorter reaction time to perturbations and delayed balance recovery compared to healthy subjects of the same age.
Annegarn et al. 2012	COPD: 79 Control: 24	Statistically significant differences were observed in COPD patients on the 6MWT relative to controls. (COPD: 494 ± 96 v/s Control: 672 ± 85.	COPD patients have an altered walking pattern during 6MWT compared to healthy subjects. These differences in walking pattern partially explain the lower 6MWD in patients with COPD.
Chien et al. 2013	COPD: 40 (Moderate / 48 severe) Control: 14	Significant differences were observed in meters run on the 6MWT between COPD patients and controls (Moderate COPD: 405 ± 14, Severe COPD: 330 ± 15 v/s control: 496 ± 27).	There are differences in 6MWT performance between COPD patients and healthy controls, in favor of controls. The greater the severity, the worse the performance.

Amorin et. al. 2014	COPD 40 Control: 40	Statistically significant differences were observed in COPD patients in the 6MWT relative to controls, being lower in COPD patients (COPD: 483 ± 70 v/s Control: 565 ± 78).	COPD patients had significantly lower exercise capacity.
Mkacher et al. 2014	COPD: 16 Control: 18	Significant differences were observed between the two groups before starting the pulmonary rehabilitation program: TUG (COPD: 15.7 ± 0.74 s vs Control 12.47 ± 0.80 s), SLS (COPD: 24.5 ± 2.28 s vs Control: 35.25 ± 7.24), BSS (COPD: 46.17 ± 1.79 vs Control: 51.31 ± 1.4).	A significant difference was observed between the two groups in all measures of balance at baseline.
Crisan et al. 2015	COPD: 29 Control: 17	The presence of COPD was associated with a significant worsening of balance tests: BBS (55 control, vs. 53 COPD), TUG (8.6 control vs. 12.3 COPD), SLS (31.1 control vs. 17.7 COPD).	According to the results, patients with moderate-severe stage COPD have a high risk of falls compared to healthy controls.
Oliveira et al. 2015	COPD: 40 Control: 25	Compared to healthy older adults, patients with COPD had a higher FOF with a mean difference of 4.8 (95% CI: 1.5 - 8.0) on the Falls Efficacy Scalee - International score. Individuals with COPD had impaired balance in the (BBS: 51.6 ± 4.2) compared to healthy subjects (BBS: 55.2 ± 1.4), p < 0.001.	Patients with COPD (moderate to severe) have an increased risk of falls and higher Falls Efficacy Scalee - International scores compared to controls. These results may guide future therapeutic strategies aimed at reducing the risk of falls.
Tudorache et al. 2015	COPD: 22 Control: 20	The presence and severity of COPD were associated with a significant decrease in 6MWD (P,0.001), SLS (P,0.001) and BBS (P,0.001) scores.	Patients with COPD have an increased history of falls, impaired balance and muscle weakness in the lower extremities.
Iwakura et al. 2016	COPD: 22 Control: 13	COPD patients demonstrated shorter SLS times (mean difference: -16.0 seconds, P=0.033) than healthy controls.	Impairments in balance and reductions in physical activity were observed in the COPD group. Deficits in balance are independently associated with physical inactivity.
Voica et al. 2016	COPD: 27 Control 17	The results point to a negative impact of the presence of COPD on all balance tests compared to controls. 6MWD (<0.001), BBS (<0.001), TUG (<0.001), SLS (<0.001).	COPD patients have greater balance impairment than their healthy controls. In addition, we observed that the Bronchitic phenotype of COPD is more likely to have falls compared to the emphysematous phenotype.
Albarrati et al. 2016	COPD: 520 Control: 150	COPD patients had a higher TUG (mean ± standard deviation: 11.5 ± 4 s) than controls (8.3 ± 1.3 s, p = 0.001); distance in the 6MWD was shorter in COPD patients (335 ± 125 m) versus control subjects (502 ± 85 m); p = 0.001.	The study confirmed that TUG, a simple and valid measure of physical performance, was higher in COPD than in controls.
Alhaddad et al. 2016	COPD: 119 Control: 58	The mean ± SD TUG time was longer in COPD patients (11.9 ± 3.7 s) versus controls (9.5 ± 1.8 s; P < 0.001). The difference remained significant when adjusted for age and sex. While 6MWD time was shorter in COPD patients (291 ± 97 m) compared to healthy controls (380 ± 76 m; P < 0.001).	TUG test time was longer in those with more comorbidities and demonstrated a relationship with recorded falls. The TUG test is a simple and reliable test to detect general functional performance in patients with COPD and may be useful in predicting the risk of falls.
Decastro et al. 2016	COPD: 47 Control: 25	17% of the COPD group obtained a unipodal support test result < 30 s, whereas 100% of the subjects in the control group completed the test. The COPD group had worse functional balance compared to the control group (TUG test: 8.5 ± 1.3 s vs. 10.3 ± 1.8 s, respectively, P < 0.001). Women with COPD performed worse on the TUG compared to men.	Individuals with COPD had worse static balance compared to healthy controls.

Oliveira et al. 2017	COPD: 26 Control: 25	COPD patients had significantly reduced scores on the BBS compared to healthy controls (51.7 ± 4.4 vs. 55.2 ± 1.4).	COPD patients had impaired functional balance performance using the BBS compared to controls.
Porto et al. 2017	COPD: 93 Control: 39	There was no significant difference in static body balance between the COPD and healthy groups (P = 0.79). Dynamic balance (BBS) was significantly lower in COPD patients (50 ± 0.69) with respect to healthy persons (54 ± 0.52). Impairment of this dynamic balance was greater in COPD than in healthy persons (35% vs. 5%). The assessed risk of falls was also higher in COPD (100%) than in healthy subjects.	Impaired dynamic balance measured with BBS was more frequent in individuals with COPD compared to healthy subjects. While in static balance there was no difference between COPD and healthy controls.
Iwakura et al. 2019	COPD: 34 Control: 16	Gait speed, step length, cadence, and acceleration magnitude were significantly lower in the COPD group than in the control group. Gait speed and stride length were significant predictors of decreased 6MWD.	The combination of gait speed, stride length and stride time is accurate in detecting poor 6MWD, which can clinically help assess the need to increase exercise capacity, muscle strength and physical activity in the routine of COPD patients.
Serrão et.al, 2020	COPD: 54 Control: 20	Statistically significant differences were observed in COPD patients on the 6MWT relative to controls. (COPD: 352 ± 122 v/s Control: 536 ± 80).	COPD patients had lower exercise capacity than healthy controls.
Gore et al.2021	COPD: 382 Control: 382	Older adults with COPD had a greater history of falls (44.9%) compared to healthy controls (34%), P= 0.003. There was no difference in tandem stance time (COPD: 24.63 ± 18.15 vs Control 26.50 ± 18.05), P = 0.45.	In older adults with COPD, cognitive function was associated with balance. Screening for cognitive function should be part of the management of falls in this population.
Jirange et al. 2021	COPD: 42 Control: 45	Individuals with COPD had decreased dynamic balance assessed by TUG (COPD: 13 (12-16) seconds vs. 12 (10-12) seconds, p < 0.01.	Individuals with COPD have reduced static balance, dynamic balance and a greater fear of falling compared to individuals without COPD.
Ozsoy et al. 2021	COPD: 35 Control: 27	During the single task the COPD patient group had a TUG of 8.85 ± 2.05 seconds, while the healthy control group had a time of 7.36 ± 1.69 seconds.	In individuals with COPD, cognitive performance impairments are more pronounced than motor performance defects during the dual task.
Schons et al 2021.	COPD: 20 Control: 16	COPD patients performed worse on most functional tests compared to the control group: TUG (COPD: 10.3 ±1.3 seconds vs. Control: 8.9 ± 12 seconds) and 6MWT (COPD: 387.6 ± 87.6 meters vs. Control: 579.8 ± 65.9 meters).	We suggest that interventions targeting rapid strength may bring improvements in functional mobility and fitness, as well as reduce fall episodes in patients with COPD.

Abbreviations: 6MWT, 6-minute walk test; BMI, body mass index; COPD, chronic obstructive pulmonary disease; BBS, Berg Balance Scale; BESTest, Balance Evaluation Systems Test; FOF, Fear of Falling; F, female; FEV_1, Forced expiratory volume in the first second; M, male; NR, not reported; TUG, Timed Up and Go; SLS, single leg stance.