Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis

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The results of this meta-analysis indicate that subjects with COPD have lower functional capacity, more history of previous falls and more risk of falling due to worse balance compared to a control group of healthy subjects https://bit.ly/3ScVEUZ

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Abstract

The objective of this study was 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 2420 individuals 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 s, 95% CI 1.79–3.43), Berg Balance Scale (mean difference: −6.57 points, 95% CI −8.31 to −4.83), static balance tests (standardised mean difference: −1.36, 95% CI −2.10 to −0.62) and the 6-min walk test (mean difference: −148.21 m, 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.

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 for Chronic Obstructive Lung Disease (GOLD), the classification of the severity of airflow limitation is based on the value of the forced expiratory volume in 1 s (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 characterised by persistent symptoms including dyspnoea, fatigue, chronic cough, and sputum production or wheezing [4, 5]. Patients with

COPD may experience episodes of exacerbations, which involve 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 healthcare 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, sex 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 are 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 3 m, 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 six 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-min 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) randomised controlled trials, quasi-randomised 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 6MWT [28], or the sit-to-stand test (STS) [29]; and 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 21 January 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; and 4) for outcomes: risk of falls OR incidence of falls OR fall rate OR accidental falls OR timed up and go OR TUG OR 6 MWT 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 (F. Vergara-Peña and P. Padilla-Acevedo) independently according to the explicit and predefined eligibility criteria. 2) Subsequently, the two reviewers (F. Vergara-Peña and P. Padilla-Acevedo) independently reviewed the full-text articles for eligibility. Any discrepancies were resolved by consensus in consultation with a third reviewer (R. Núñez-Cortés).

Data extraction

The data extraction was completed independently by each reviewer (P. Padilla-Acevedo, F. Vergara-Peña and C. Espinoza-Bravo) following a standardised form. Disagreements were resolved by a third reviewer (R. Núñez-Cortés). 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 (%), body mass index ($kg \cdot m^{-2}$), FEV_1, clinical assessment test, outcomes (comparative measure between groups) and conclusion. If any relevant data were not included in the study 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 and 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 <50% of the elements were met [31]. The quality assessment was evaluated independently by four reviewers (P. Padilla-Acevedo, F. Vergara-Peña, S. Mollà-Casanova and C. Espinoza-Bravo) and a fifth reviewer was consulted to resolve any discrepancies (R. Núñez-Cortés).

Quantitative analysis of the results

The RevMan 5.3 software (The Cochrane Collaboration, Oxford, UK) 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% and 40% might not be important, while between 30% and 60% is moderate heterogeneity, between 50% and 90% is substantial heterogeneity and between 75% and 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

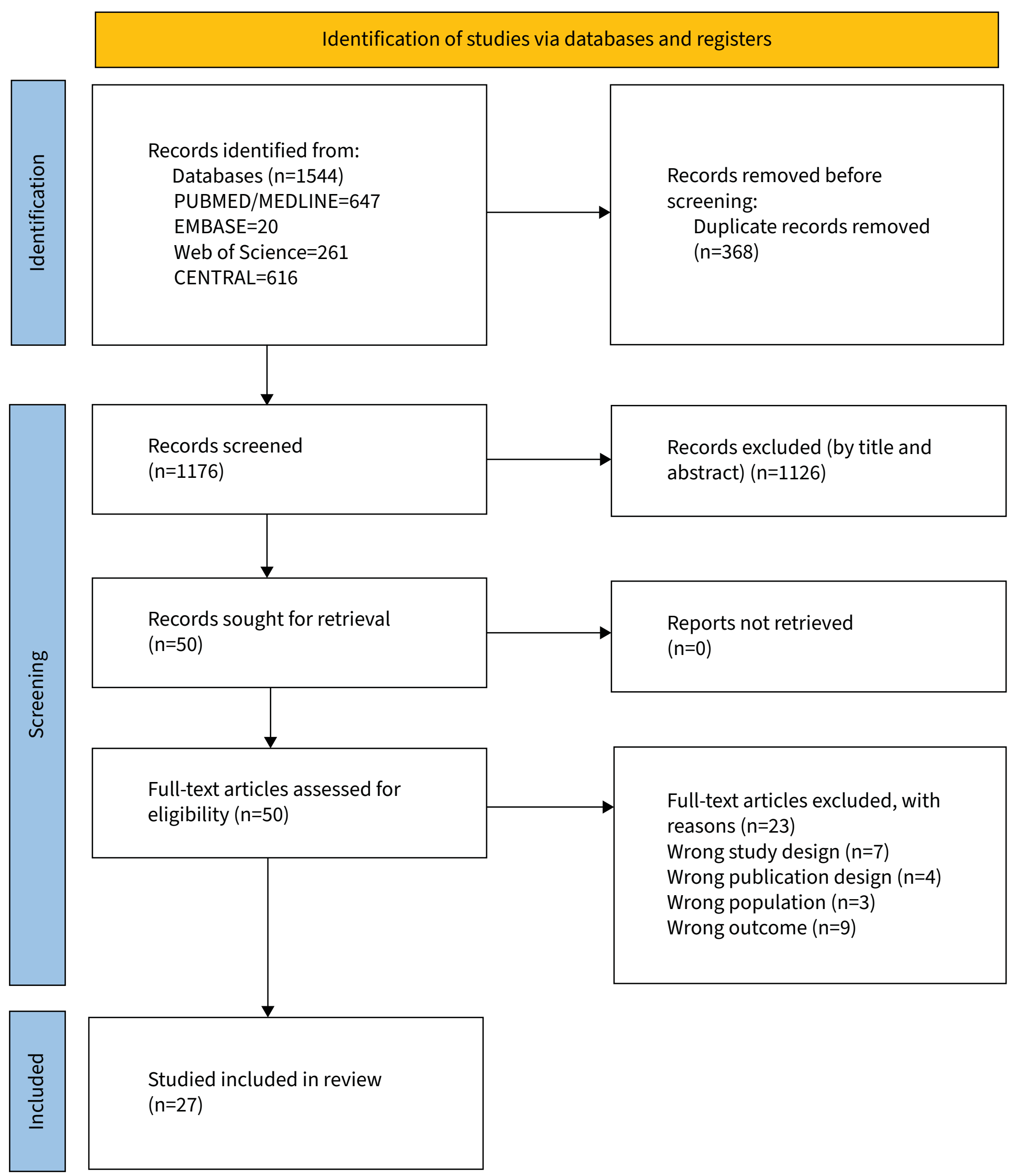

FIGURE 1 Study selection process.

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 23 were cross-sectional studies. A total of 2420 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, 11 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, 17 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 summarised in supplementary table S1.

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 *versus* 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%).

Timed Up and Go

11 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 *versus* Control: 412 participants). The overall result of the meta-analysis was in favour of the control group (mean difference 2.61 s, 95% CI 1.79–3.43) (figure 3b). The heterogeneity among the studies was considerable (I^2=93%).

Berg Balance Scale

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 *versus* 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 *versus* Control: 504 participants). The overall result of the meta-analysis was in favour of the control group (SMD −1.36, 95% CI −2.10–0.62) (figure 3d). The heterogeneity among the studies was considerable (I^2=92%).

6-min walk test

17 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 *versus* Control: 610 participants). The overall result of the meta-analysis was in favour of the control group (mean difference −148.21 m; 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

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TABLE 1 Characteristics of the included studies

Study, year (country)	Study design	n (M/F)	Age years	BMI kg·m^{-2}	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 (Netherlands)	Cross-sectional	COPD: 79 (47/32) Control: 24 (15/9)	COPD: 64.3±8.9 Control: 63.7±5.9	COPD: 24.7±4.5 Control: 25.8±3.8	COPD: 53.5±18.7 Control: 124.9±21.0	6MWT
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 (UK)	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 (UK)	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

Continued

TABLE 1 Continued

Study, year (country)	Study design	n (M/F)	Age years	BMI $kg \cdot m^{-2}$	FEV_1 % predicted	Outcome
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 (USA)	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

Data presented as mean±SD unless stated otherwise. Abbreviations: M: male; F: female; BMI: body mass index; FEV_1: forced expiratory volume in 1 s; COPD: chronic obstructive pulmonary disease; COPD (NO): no supplemental oxygen; COPD (WO): COPD with supplemental oxygen; NR: not reported; TUG: Timed Up and Go; 6 MWT: 6-min walk test; BBS: Berg Balance Scale; GOLD: Global Initiative for Chronic Obstructive Lung Disease; BESTest: Balance Evaluation Systems Test; ABC: activity-specific balance of confidence scale; SLS: single leg stance; FES-I: Falls Efficacy Scale - International.

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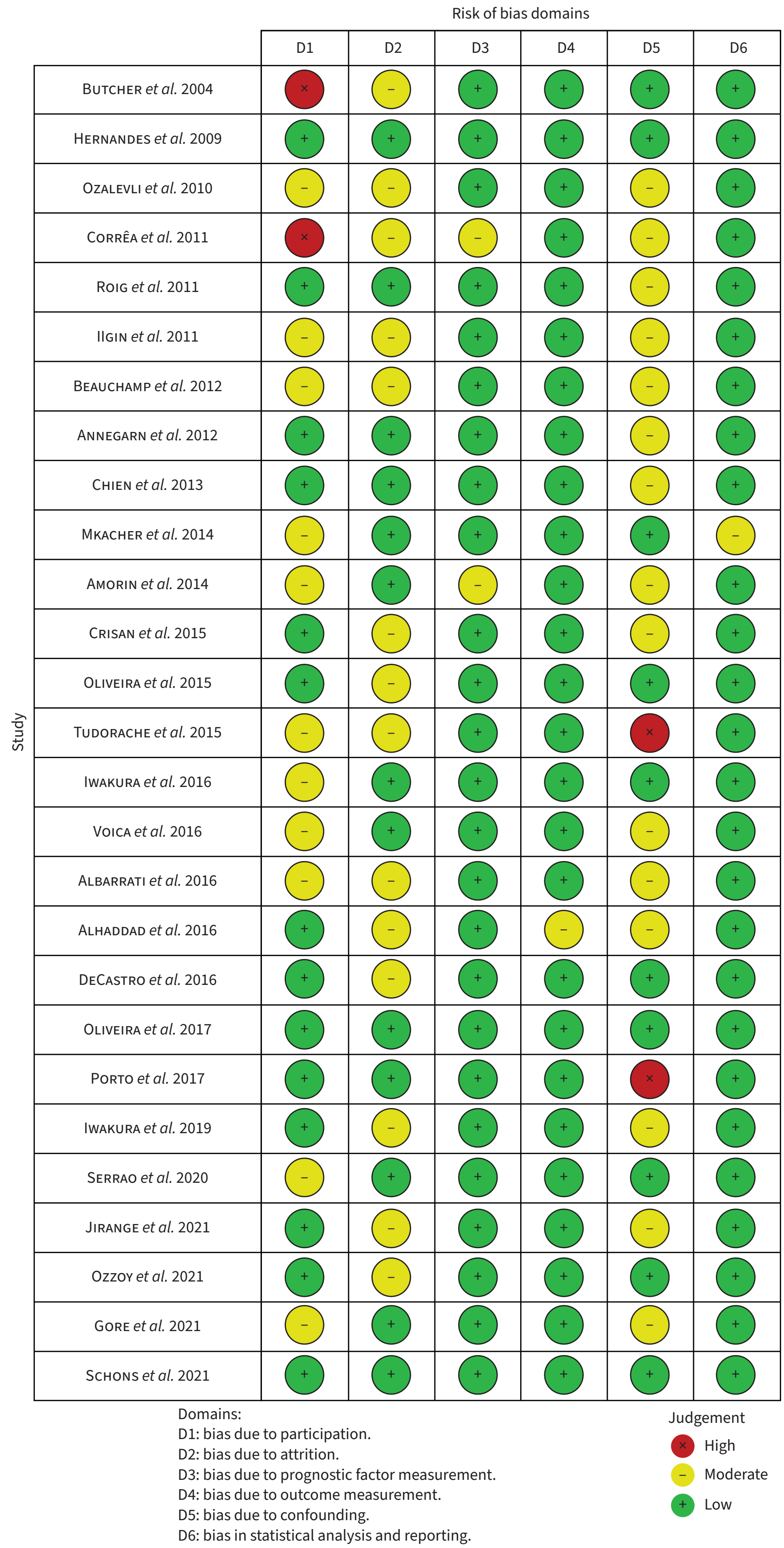

FIGURE 2 Summary of risk of bias assessment using the Quality in Prognosis Studies (QUIPS) tool.

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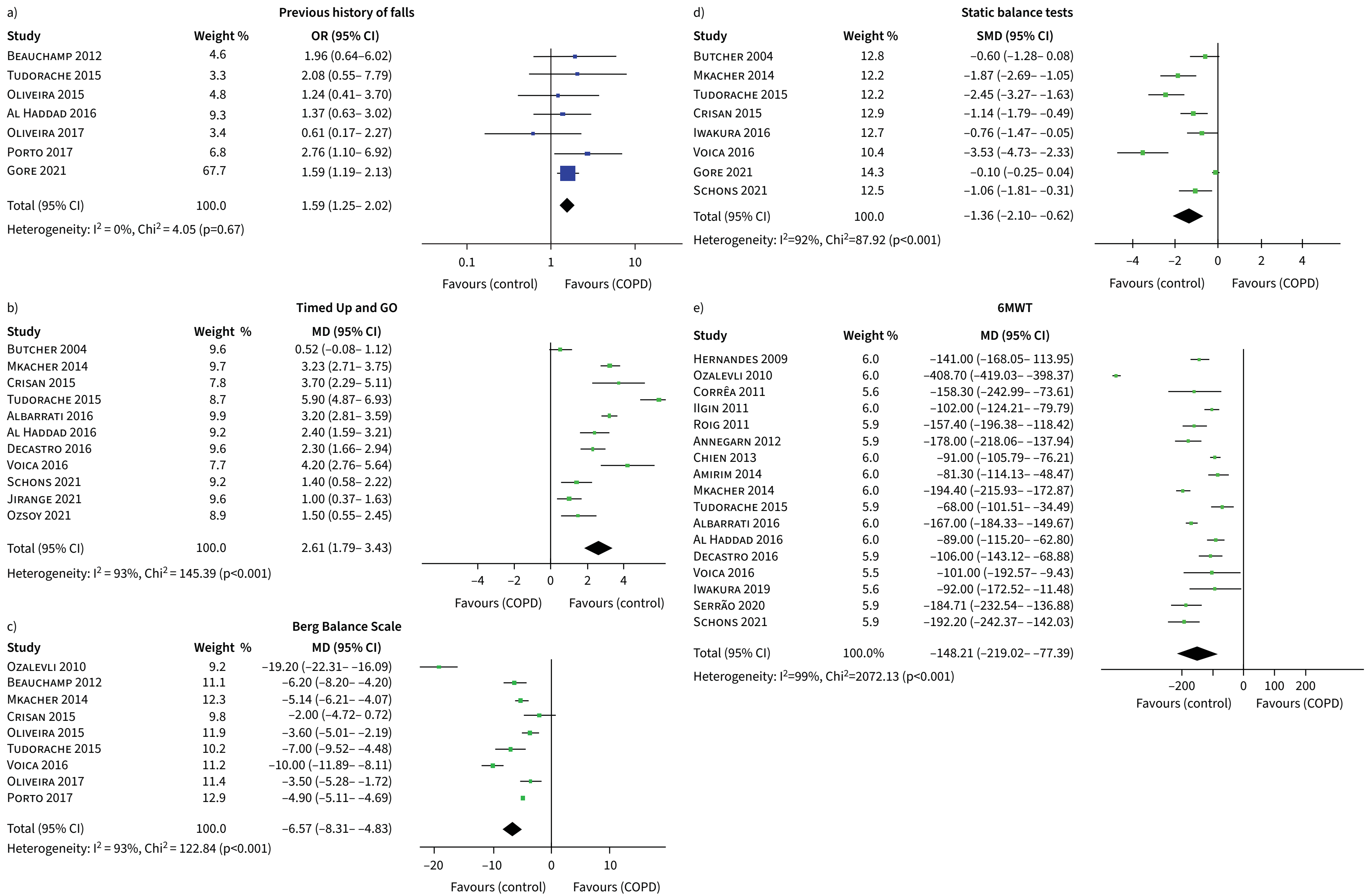

FIGURE 3 Quantitative synthesis. a) Forest plot of the comparison of history of previous falls between people with COPD and healthy controls; b) forest plot of the comparison of Timed Up and GO (TUG) between people with COPD and healthy controls; c) forest plot of the comparison of Berg Balance Scale (BBS) between people with COPD and healthy controls; d) forest plot of the comparison of balance static tests between people with COPD and healthy controls; 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. OR: odds ratio; 95% CI: 95% confidence interval; COPD: chronic obstructive pulmonary disease; MD: mean difference; SMD: standardised mean difference; 6MWT: 6-min walk test.

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 s [66]. Therefore, the differences observed with healthy subjects were above the threshold of clinical relevance defined in the literature (mean difference 2.82 s). 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 m [67]. Therefore, the mean differences observed with the control group of 148 m 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 values 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 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 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.

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