Effects of Exercise-based Management on Motor Symptoms in Parkinson's Disease - A Meta-analysis

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ABSTRACT

Parkinson's disease (PD) is the second most common neurological illness after Alzheimer's disease. According to research, medication alone can give palliative alleviation; however, freezing of gait (FOG) and balance can be treated with physical therapy. This meta-analysis aims to bridge gaps about exercise-based therapy's impact on balance and FOG in patients with PD. Google Scholar, CINHAL, Medline, PubMed, and PEDro were searched for 2016-2021 citations using the PIOD paradigm. Pooled effect size mean and SD were analysed using a fixed and random effects model. A total of 21 trials were included in this review, with SMD=0.60 and p=0.0007 utilising BBS. The pooled analysis revealed statistically significant impacts on exercise-based management in the experimental group. With SMD=0.87 and p<0.00001 using Mini-BESTest, the pooled analysis revealed that exercise-based management was also effective on balance in the experimental group. The fixed effect model of FOG in terms of SMD was used to draw the pooled effects of FOG in terms of SMD and FOG in terms of SMD (0.21; 95 percent CI -0.01 to 0.44; p=0.06). According to this research, several physiotherapy approaches such as exergaming, gamepad systems, virtual reality, gait exercises, and core training, help Parkinson's patients regain balance and FOG.

Key Words: *Parkinson's disease, Physical therapy techniques, Neurological rehabilitation, Balance, Freezing of gait, Motor symptoms.*

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INTRODUCTION

Worldwide neurological diseases are the second greatest cause of morbidity and mortality.[1] Parkinson's disease (PD) is the second most common age-related neurodegenerative disorder after Alzheimer's disease.[2] It affects around 6 million individuals worldwide and is expected to double in the next 20 to 30 years.[3,4] According to the American Parkinson's Disease Association (APDA), one million people live with PD.[5] However, in 2016, the United States (US) reported 800,000 PD patients, the highest number of PD patients in the world, while the United Kingdom (UK) reported 100,000 cases, the lowest number of PD patients in the world. If present trends continue, the number of cases is predicted to rise in US and UK by 2026.[6] According to the Pakistan Parkinson's Society, around 450,000 people in Pakistan are affected by Parkinson's disease.[7] However, Pakistan has a high prevalence of PD among those aged 70 to 79 years, with males being more affected than females.[8,9] Furthermore, PD is a degenerative condition with several motor and non-motor symptoms, which include tremors, stiffness, and bradykinesia as motor symptoms. In contrast, constipation, cognition and disturb sleep as non-motor symptoms (NMS).[10]

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Poor balance is a significant symptom of PD that manifests early in the illness[11] and affects approximately 75% of individuals.[12]

Freezing of gait (FOG) is an accomplished predictor of falls and has a significant effect on mobility.[13] According to Caroll *et al*., FOG affects up to 50% of persons with PD.[14]

A growing body of scientific data demonstrates the benefits of rehabilitation treatment for PD.[15] However, according to a recent comprehensive analysis, prescribed exercise performed at home has minimal effect on improving balance in patients with PD.[16] A meta-analysis of 191 studies published in 2020, concluded that motor symptoms including balance and gait were improved with dance, nordic walking, balancing and martial arts training, and exergaming in PD patients.[17]

Presently, there is no verified data on pharmaceutical therapy to prevent or postpone the disease development. However, a previous study discovered that physical exercise might be combined with pharmacological therapy to control disease symptoms such as balance and gait.[18,19] However, a comprehensive assessment of various physical therapies in PD patients is still missing.

The purpose of this meta-analysis was to examine the effects of various exercise therapies on balance and FOG among Parkinson's patients.

METHODOLOGY

The current meta-analysis was performed in accordance with the guidelines of Preferred Reporting Items for Systematic

Reviews and Meta-Analysis (PRISMA).[20] The protocol and features of the study were registered in the international database of systematic review and meta-analysis PROSPERO (register number: CRD42021284371).

The studies were chosen using the PIOD approach, which stands for Population, Intervention, Outcome, and Design.[21] Participants aged 60 years and above having PD stage I-IV with impaired balance and FOG were included in this meta-analysis. Moreover, biofeedback gamepad-based training, exergaming, virtual reality (VR), curved walking training, slackline training, action observation training, obstacle aquatic therapy, argentine tango (AT), resistance training, adapted resistance training, and dance therapy are among the interventions being studied and BBS, TUG test, Mini-BESTest, FOG-Q, and nFOG questionnaire were used as an outcome measure. Only randomised controlled trials (RCTs; parallel) were included in this study. Studies not written in the English language or did not have a translation available were excluded.

Two independent researchers conducted a search strategy from September 2021 to April 2022, in the following databases; Ovid, Google Scholar, CINHAL, PubMed, PEDro Web of Science, and Scopus for the articles published between 2016 and 2021. Different search strategies were used where the following keywords (MeSH) are combined with the Boolean Operators (AND, OR and NOT); "physical therapy" OR "physiotherapy" OR "physiotherapy Exercises") AND (Parkinson's Disease" OR "PD") AND ("balance") AND ("freezing of gait" OR "FOG") AND "motor symptoms". However, in order to cater the unpublished articles a thorough inspection was carried out in the bibliographical list of incorporated papers and previously issued reviews.

Article selection and data extraction were carried out by two independent reviewers in accordance with a data extraction checklist and Cochrane criteria.[22,23] Several discussions session were conducted between the independent reviewers. If any disagreement occurred then a meeting was scheduled to address the concerns and take opinions with 3rd, 4th, and 5th reviewers. Research design, H & Y staging criteria, intervention type, intervention characteristics, and outcome measures were extracted from the included studies using a standard data-recording spreadsheet.

RevMan 5.4.1 statistical software was used to examine the data for the meta-analysis. The review was carried out with the goal of determining the balance and FOG as outcome metrics. For both the physiotherapy treatment and control groups, RCTs including baseline and post-treatment data were introduced. The pooled effect size estimates were evaluated using fixed effects and random effects model. In the experimental and control groups, the mean, standard deviation, and 95 percent confidence intervals (95 percent CIs) for balance and FOG scores were used. The I^2 statistic was used to quantify heterogeneity in the model, with I^2 values ranging from 0% to 40% showing no heterogeneity, 30% to 60% showing moderate heterogeneity, 50% to 90% showing substantial heterogeneity, and 75 percent to 100% showing considerable heterogeneity.[24]

When there was modest to moderate heterogeneity, a fixed model was estimated, and when there was substantial to large heterogeneity, a random-effect model was computed.[25] For all analyses, the effect size (ES) was set to be small (0.2 to 00.49), moderate (0.5 to 0.79), and large (0.8 or above), with $p<0.05$ considered statistically significant.[26]

Selection bias, *i.e*. randomisation and allocation concealment; performance bias, *i.e*. blinding; attrition bias, *i.e*. incomplete outcome data; reporting bias, *i.e*. selective reporting of outcome and other potential biases were used to assess the quality and risk of the included studies.[24] Green indicated a lower risk of bias, red indicated a greater risk of bias, and yellow indicated the unknown risk of bias (Figures 2 and 3).

RESULTS

Two hundred and one studies were retrieved from electronic databases including Medline, BioMed Central, PubMed, Cochrane, and Google Scholar database, 99 of which were duplicates. A total of 51 full-text articles were considered for inclusion. Finally, this meta-analysis includes 21 published RCTs from 2016 to 2021 (Figure 1).

Tables I and II provide a comprehensive review of the trials as well as participant characteristics on balance and FOG.

This meta-analysis included eleven studies that focused on balance in Parkinson's patients.[27-37] BBS was used in 4 out of 11 studies to assess balance in PD patients.[28,31,32,33] A random effect model was chosen on heterogeneity (I^2=11%). The pooled analysis revealed that physiotherapy treatments had substantial effects (SMD 0.60; 95 percent CI 0.25 to 0.94; p=0.007) and a large ES= 3.38 (Figure 2). Exergaming, gamepad systems, and virtual reality were found to be useful in improving balance in PD patients using BBS.[28,31,32,33]

The TUG test was used in five out of eleven studies to assess balance in PD patients.[29,30,34,36,37] The findings of the pooled analysis on random-effect revealed that physiotherapy interventions had no significant impacts (SMD -0.30; 95 percent CI -0.84 to 0.25; p=0.29) on heterogeneity (I2=63%), however, the forest plot revealed that experimental group is more effective, with an ES=1.07 (Figure 2). The TUG test revealed that physiotherapy therapies such as VR, home-based step training, LSVT, and trunk resistance exercises were ineffective in improving balance in PD patients.[29,30,34,36,37]

The Mini-BESTest was used in two out of eleven studies to assess balance in PD patients.[27,35] The pooled analysis revealed substantial effects of physiotherapy interventions (SMD 0.87; 95 percent CI 0.53 to 1.21; p<0.001) with a large ES=4.96 with no heterogeneity (Figure 2). Gait exercises and core training have been demonstrated to help patients with Parkinson's disease improve their balance.[27,35]

The pooled analysis of total 17 studies revealed substantial effects of physiotherapy interventions with SMD=0.29 at 95% CI (-0.09 to 066; p<0.001) with ES=1.51 (Figure 2).

Table I: Summary of the studies on balance that were included.

Author	Design	Hoehn and Yahr Stages	On-Time/Off Time	Groups	Intervention	Outcome Measures
Shih *et al*. 2016	RCT	1-3	ON time	EG (n=10)	For 8 weeks, received exergaming for 50 minutes per session, twice a week.	BBS
				CG (n=10)	For 8 weeks, received conventional balancing training for 50 minutes per session, twice a week.	
Yang *et al*., 2016	RCT	2-3	ON time	EG (n=11)	For 6 weeks, received VR training for 50 minutes per session, twice a week.	TUG
				CG (n=12)	For 6 weeks, participants received traditional balance training twice a week for 50 minutes each session	
Carpinella *et al*., 2017	RCT	2-4	OFF time	EG (n=17)	For 7 weeks, received exercises via a Gamepad device for 45 minutes per session, three times per week.	BBS
				CG (n=20)	For around 7 weeks, participants received traditional balance exercises for 45 minutes per session, three times per week.	
Gandolfi *et al*., 2017	RCT	2.5-3	ON time	EG (n=38)	For 7 weeks, received VR telerehabilitation for 50 minutes per session, three times per week.	BBS
				CG (n=38)	For 7 weeks, received SIBT for 50 minutes per session, three times per week.	
Ribas *et al*., 2017	Pilot RCT	1-3	ON time	EG (n=10)	For 12 weeks, received exergaming through Wii Fit games for 30 minutes every session, twice a week.	BBS
				CG (n=10)	Received a standard exercise	
Song *et al*., 2018	RCT	Not mentioned	ON time	EG (n=31)	For 12 weeks, received home-based step training using video-game technology for 15 minutes per session, three times per week.	TUG
				CG (n=29)	Maintain your normal routine.	
Wallén *et al*., 2018	RCT	2-3	ON time	EG (n=51)	Balance and gait exercises were given three times a week for 10 weeks, lasting 60 minutes each time	Mini-BESTest
				CG (n=49)	Received dual-tasks	
Feng *et al*., 2019	RCT	2.5-4	ON time	EG (n=14)	VR training for 12 weeks, 45 minutes per session, 5 days a week	TUG
				CG (n=14)	For 12 weeks, received traditional physical therapy for 45 minutes per session, 5 days a week	
Cabrera-Martos *et al*., 2020	RCT	2-3	ON time	EG (n=22)	For eight weeks, received core training for 45 minutes every session, three times per week.	Mini-BESTest
				CG (n=22)	For eight weeks, participants received traditional workouts for 45 minutes every session, three times per week.	
Chogle *et al*., 2020	RCT	1-3	Not mentioned	EG (n=16) CG (n=16)	For four weeks, received conventional treatment as well as LSVT BIG therapy four times a week Conventional treatment	TUG
Youm *et al*., 2020	RCT	1-3	ON time	EG (n=10)	For 12 weeks, received a progressive trunk resistance and stretching workout programme that lasted 60-90 minutes per session and was done three times per week.	TUG
				CG (n=7)	Continue their daily activities	

SIBT: Sensory integration balance training program; Mini-BESTest: Mini-balance evaluation system test; LSVT: Lee Silverman voice therapy.

This meta-analysis included ten studies that assessed FOG in Parkinson's disease patients.[38-47] Seven of the ten investigations used FOG-Q to assess FOG[38,39,47,42-45] while three used FOG-Q to measure FOG.[40,41,46] There is moderate heterogeneity (I^2=47%) and a fixed effect model was used. In a pooled analysis, physiotherapy therapies produced non-significant effects (SMD 0.21; 95 percent CI -0.01 to 0.44; p=0.06), but a substantial ES=1.90 (Figure 3). Treadmill training[45], slackline training,[44] AOT,[38,41,42] CWT,[39] dance therapy,[40,43] aquatic therapy[47], modified resistance training[46] and various other physiotherapy therapies were not found to be useful in improving FOG in PD patients (Figure 2).

Cochrane risk of bias of assessments of included studies is presented in Figures 4 and 5.

DISCUSSION

PD patients' motor symptoms, such as balance and FOG, can be improved by exercise-based treatment, and this meta-analysis of RCTs is the first to examine the methodological quality and important results of RCTs published in the previous six years (2016 to 2021). This meta-analysis examines 787 Parkinson's patients from 21 high-quality studies, 11 trials on balance, and 10 trials on FOG.

A number of studies have demonstrated that, while no cure for PD has yet been discovered, adequate management approaches that combine both pharmacotherapy and physiotherapy can help to slow down the course of the disease.[27] Furthermore, according to various studies, pharmacotherapy alone may be effective in providing palliative relief; however, concerns such as gait impairment and postural sway can be addressed with appropriate physical rehabilitation treatments.[28]

The main findings indicated that exercise-based treatment improved motor symptoms, such as balance and FOG, in Parkinson's patients in stages I through IV. The BBS, TUG, and Mini-BESTest were used as outcome measures for balance recovery, and pooled analysis indicated that the BBS had a statistically significant effect on exercise-based management in the experimental group (Figure 4).[28,31-33]

Table II: Summaries of the studies on FOG.

Author	Design	Hoehn (H) and Yahr (Y) Stages	On-Time/Off Time	Groups	Intervention	Outcome Measures
Schlick *et al*., 2016	Pilot RCT	2-4	ON time	EG (n=12)	Within 5 weeks, received visual cues with treadmill training for 2-3 sessions each week and a total of 12 sessions.	FOG-Q
				CG (n=11)	Within 5 weeks, received only treadmill training for 2-3 sessions each week and a total of 12 sessions.	
Santos *et al*., 2017	RCT	1-3	ON time	EG (n=11)	For 6 weeks, received a slackline training programme that lasted 23 minutes for each session and included two sessions per week	FOG-Q
				CG (n=11)	Carry on with their normal routines	
Agosta *et al*., 2017	RCT	1-3	ON time	EG (n=12)	For four weeks, received AOT for 60 minutes per session, three times per week	FOG-Q
				CG (n=13)	Landscape was given to me for 60 minutes per session, three times a week for four weeks	
Cheng *et al*., 2017	RCT	1-3	ON time	EG (n=12)	CWT was given for 40 minutes per session for a total of 12 sessions over the course of 4-6 weeks	FOG-Q
				CG (n=12)	Trunk exercises were given for 40 minutes every session for a total of 12 sessions over the course of 4-6 weeks	
Pelosin *et al*., 2018	RCT	2-3	ON time	EG (n=32)	For 5 weeks, received AOT for 45 minutes per session, twice a week.	FOG-Q
				CG (n=32)	For 5 weeks, received LOT for 45 minutes per session and twice a week.	
Rocha *et al*., 2018	Pilot RCT	1-4	Not mentioned	EG (n=10)	For eight weeks, received dance therapy (Argentine tango) once a week for 60 minutes	FOG-Q
				CG (n=11)	For eight weeks, received dance therapy (mixed genre) for 60 minutes per session, once a week	
Zhu *et al*., 2018	RCT	2-3	Not mentioned	EG (n=23)	For six weeks, received aquatic therapy for 30 minutes every session, five times per week.	FOG-Q
				CG (n=23)	For 6 weeks, received obstacle aquatic therapy for 30 minutes every session, 5 times per week.	
Mezzarobba *et al*., 2018	Pilot RCT	1-3	ON time	EG (n=12)	For 8 weeks, received AO plus sonification for 60 minutes per session, twice a week.	NFOG-Q
				CG (n=10)	For eight weeks, participants were given visual cues for 60 minutes per session, twice a week.	
Silva-Batista *et al*., 2020	RCT	3-4	ON time	EG (n=20)	For 12 weeks, received tailored resistance training for 80-90 minutes three times a week.	NFOG-Q
				CG (n=20)	For 12 weeks, received typical motor rehabilitation for 80-90 minutes three times a week	
Frisaldi *et al*., 2021	Pilot RCT	1-2	ON time	EG (n=19)	For 5 weeks, received traditional physiotherapy followed by a 120-minute dancing lesson three times a week.	NFOG-Q
				CG (n=19)	For 5 weeks, received traditional physiotherapy for 60 minutes every session, three times per week.	

AOT: Action observation training; CWT: Curved-walking training: LOT: Landscape observation therapy.

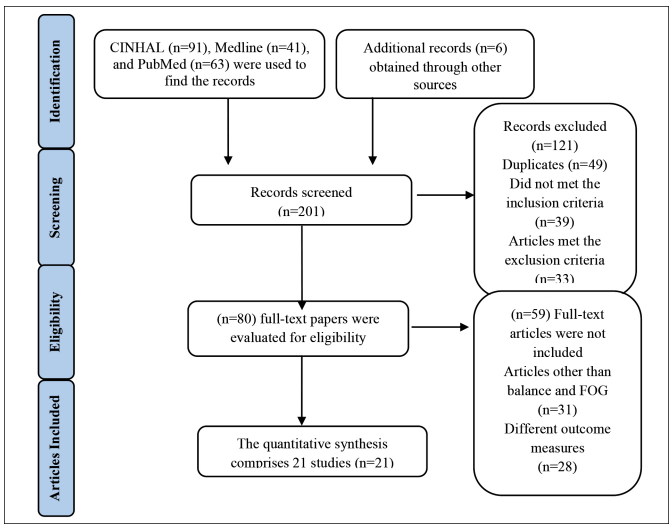

Figure 1: PRISMA flowchart for study selection.

Moreover, The Mini-BESTest demonstrated statistically significant effects on exercise-based balance management in the experimental group, with SMD=0.87 and p<0.001 (Figure 2) in the pooled analysis.[27,35] In this study, the FOG-Q and nFOG-Q were used as outcome measures for FOG recovery, and a pooled analysis demonstrated statistically significant effects on exercise-based management when compared to the control group, with an SMD of 0.21 and a p-value of 0.06 (Figure 3).[38-47]

In stage I-IV, both the BBS (Figure 2)[28,31-33] and Mini-BESTest (Figure 2)[27,35] showed significant influences on balance. Although FOG-Q and nFOG-Q were shown to have very small impacts on stages I-IV, they were discovered to have a considerable ES (Figure 3). In comparison to this research, a review article released in 2020 discovered that numerous physiotherapy therapies effectively improved FOG compared to a control group.[48] A meta-analysis was conducted by Klamroth *et al.*, in 2016 which showed that the physiotherapy interventions had significant effects in improvement of postural instability in Parkinson's patients.[49]

In this study, the PRISMA guidelines were followed.[50] The potential for bias was utilised to evaluate the quality of the trials, and all studies had a greater risk of participant and employee blinding bias [27-37] and the majority of balancing studies had lost participants.[28,33-37]

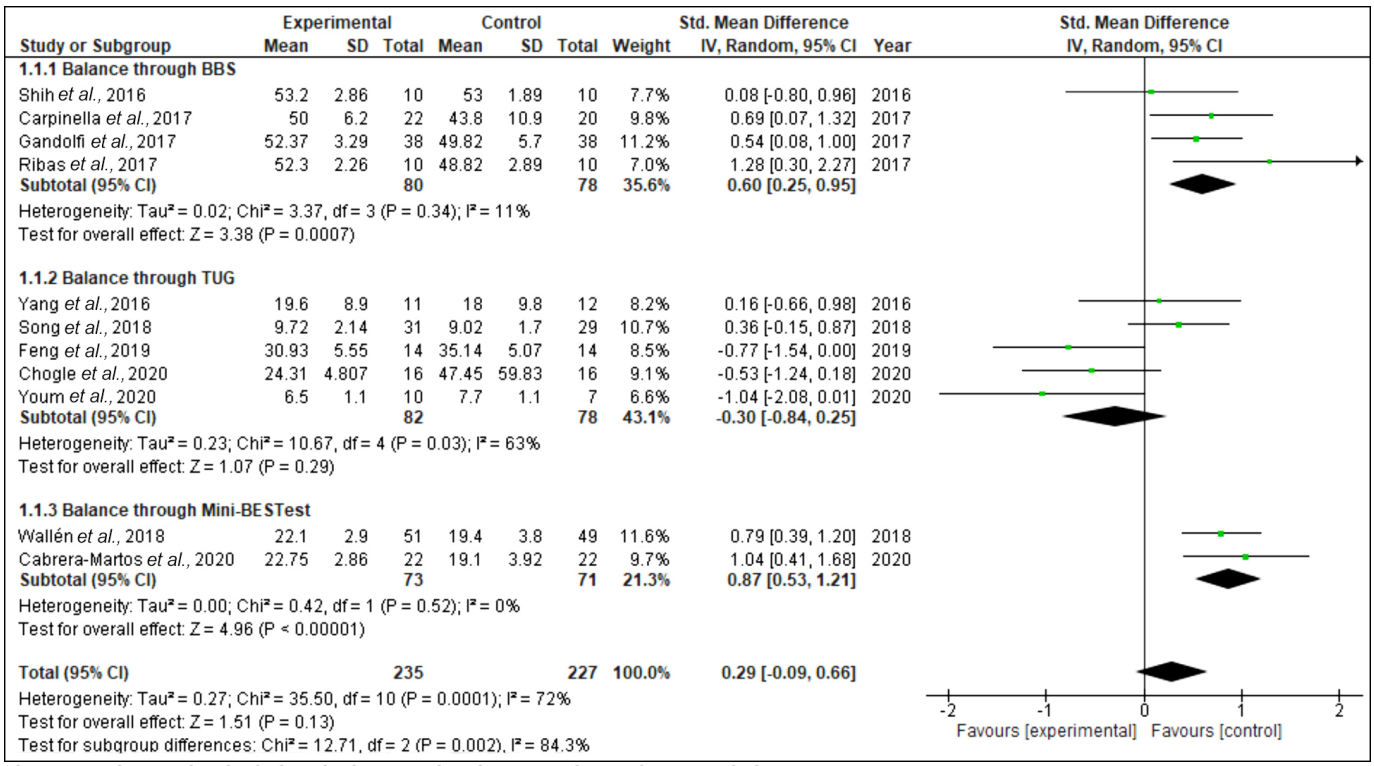

Figure 2: A forest plot depicting the impact of various exercise regimens on balance.

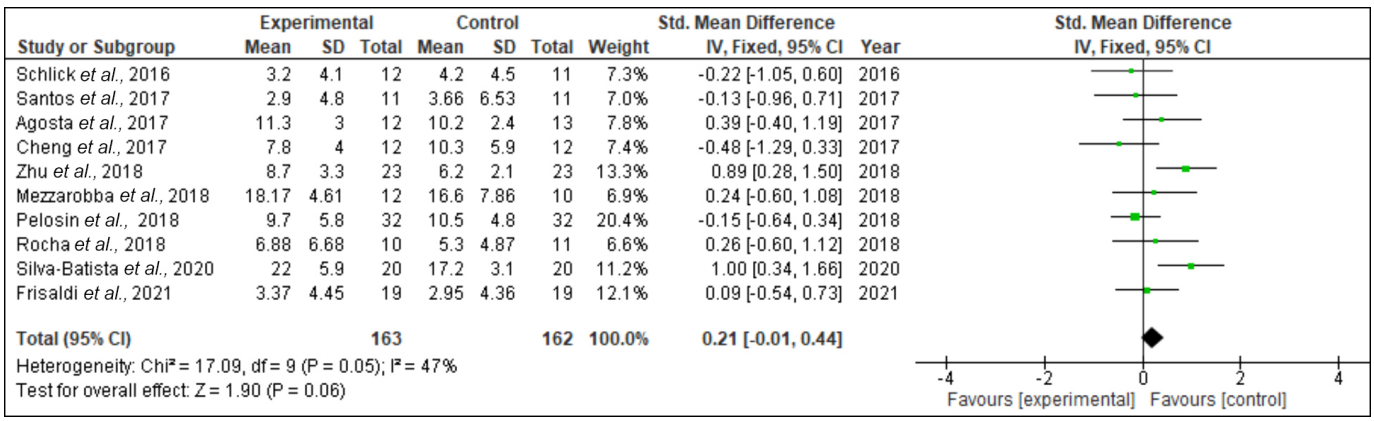

Figure 3: Effects of various exercise therapies on FOG as a forest plot.

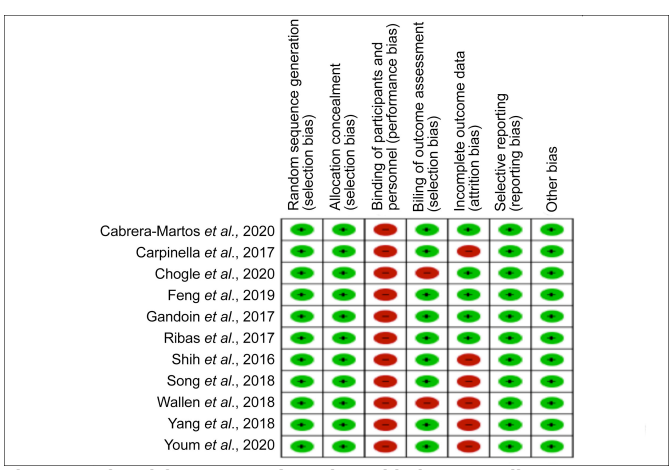

Figure 4: Bias risk summary for selected balance studies.

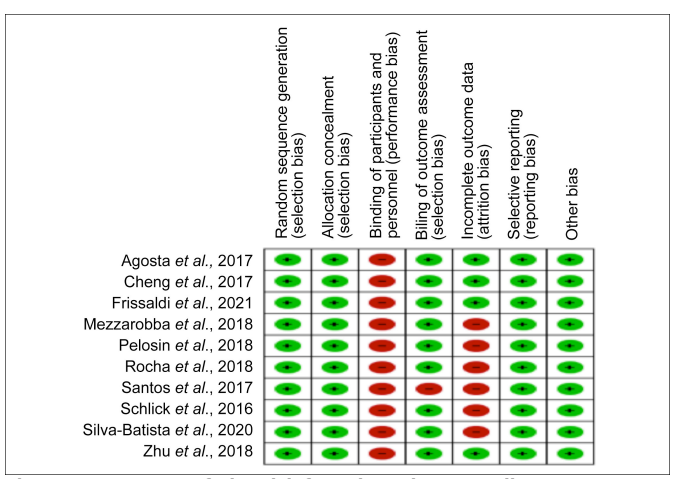

Figure 5: Summary of Bias risk for selected FOG studies.

However, FOG studies have a greater risk for bias in terms of participant and personnel blinding[38-47] and inadequate outcome data.[43-46] The reasons for dropouts were patients hospitalised due to their illnesses and travel to another city. According to the researcher's knowledge, there are few studies on Parkinson's patients' balance and FOG. The included studies focused on a range of physiotherapy therapies and outcome measures, as opposed to a single intervention and outcome measure, which is a limitation of the study.

This analysis of RCTs (2016-2021) employing valid and trustworthy instruments such as the BBS, TUG, Mini-BESTest, FOG-Q, and nFOG-Q has the benefit of being high-quality research in the hierarchy. It was an extensive study with stringent selection criteria and a thorough data extraction strategy.

Moreover, this high-quality research emphasises biofeedback therapy in managing balance and FOG in Parkinson's patients with a larger sample size providing enjoyable, good exercise adherence and cost-effective treatment in Parkinson's patients. The future study will focus on individual H & Y staging criteria.

CONCLUSION

This review concluded that various physiotherapy treatments, such as exergaming, gamepad systems, virtual reality, gait exercises, and core training, are beneficial for the rehabilitation of balance and FOG among stage I-IV in patients with PD.

COMPETING INTEREST:
There were no potential competing interests that were relevant to this article.

AUTHORS' CONTRIBUTION:
FH, SIF, BH: Conception of study design and interpretation of data.
FH, IAK: Drafting and revising the manuscript critically for important intellectual content.
BH, ZKA: Proofreading of the final version of the manuscript.
All the authors have approved the final version of the manuscript to be published.

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