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The Effects of Exercise Interventions on Balance Capacity in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis

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Abstract

The effect of exercise intervention on balance capacity among type 2 diabetes mellitus (T2DM) patients has not been evaluated. The objective of this systematic review and meta-analysis is to investigate the effect of exercise intervention on balance capacity among T2DM patients compared to the control group (usual care, waitlist, no-treatment, education). We conducted a comprehensive literature search through PubMed, EMBASE, Physiotherapy Evidence Database (PEDro), Cochrane library, Web of Science (WOS) from inception to August 2020. The literature language was limited to English. Randomized controlled trials (RCTs) or quasi-experimental (Q-E) trials that examined the effect of exercise intervention on balance capacity among T2DM patients were included. We used the standard methods of meta-analysis to evaluate the outcomes of exercise intervention for balance capacity of T2DM patients. A total of 14 trials (11 RCTs and 3 Q-E trials) involving 883 participants were eligible. The meta-analysis of some studies demonstrated that exercise intervention could significantly improve Berg Balance Scale (BBS) (MD = 2.56; 95%CI [0.35, 4.77]; $P = .02$), SLST (Single Leg Stance Test) under the eyes-open (EO) condition (MD = 3.63; 95%CI [1.79, 5.47]; $P = .0001$) and eyes-close (EC) condition (MD = 0.41; 95%CI [0.10, 0.72]; $P = .01$) compared to control group. There was no significant difference in Time Up and Go Test (TUGT) (MD = −0.75; 95%CI [−1.69, 0.19]; $P = .12$) and fall efficacy (SMD = −0.44; 95%CI [−0.86, −0.01]; $P = .05$). Narrative review of some studies indicated that exercise intervention could improve postural stability measured by Sensory Organization Test (SOT) and Center of Pressure (COP) variables, etc. This systematic review and meta-analysis summarized that exercise intervention could improve balance capacity in T2DM patients. However, further studies with high quality are required to evaluate its effect.

Keywords

exercise, balance, type 2 diabetes mellitus, systematic review

What do we already know about this topic?
The evidence of exercise interventions for balance capacity related outcomes among patients with diabetes were limited, especially in laboratory balance tests.
How does your research contribute to the field?
We found that exercise interventions could significantly improve Berg Balance Scale and Single Leg Stance Test, and also comprehensively summarized about exercise intervention improve postural stability measured by laboratory tests.
What are you research's implications toward theory, practice, or policy?
We summarized that exercise intervention could improve balance capacity in T2DM patients. However, further studies with high quality are required to evaluate its effect.

Introduction

According to the survey of the International Diabetes Federation,[1] there were about 451 million patients with diabetes in the world in 2017, the number of patients was increasing, and more than 90% of them were type 2 diabetes mellitus (T2DM). It was reported that the incidence of falls in older patients with diabetes mellitus was 39%,[2] which was 3 times higher than that in normal people.[3] The risk of falls in T2DM patients was 1.19 times higher than that in patients without diabetes,[4] the overall fall rate of 1 DM patients could reach 1.25 times/year.[5] Fall is the main cause of fatal injury in the elderly, and it is also the most common cause of non-fatal injury related hospitalization in the elderly.[6] In 2016, the National Council on Aging reported that more than 25% of people aged over 65 fall every year, with an average of 1 elderly person falling to the emergency room every 11 s and an average of 1 elderly person dying directly or indirectly every 19 min caused by the fall.[6] 29 million older people have experienced fall in the United States in 2014, and the number are expected to be 74 million by 2030.[6] The total economic loss caused by falls was $34 billion in 2013 and is expected to reach $67.7 billion in 2020.[6] A review[7] of 93 studies on falls showed that the hospitalization cost for fall-related injuries for the elderly in China with an average cost of $1768, and the cost were $29,562 for elderly Americans.[8] The fall caused by DM brings serious negative effects on patients, families, public health system and society, including economic, functional and psychological aspects.

Diabetes is strongly associated with an increasing risk of falling, and impaired balance function is the main cause of falls.[9,10] More and more elderly people are afraid of falling, thus limiting their daily activities and social behavior, leading to further physical decline, depression, social isolation, and feelings of helplessness. The microvascular complications in the nervous system were common in DM patients, diabetic peripheral neuropathy (DPN) is the result of destruction and degeneration of peripheral somatic nerves which affects 30% to 50% individuals with diabetes.[11] Impaired balance capacity of patients with diabetes has historically been attributed to DPN, however, balance dysfunction were also found in those DM patients without DPN.[12,13] A significant positive correlation was found between fall risk/rate and fall efficacy (fall fear or balance confidence) in the elderly,[14] and there were significant differences in balance function measures between the elderly with higher fall efficacy and those with lower fall efficacy.[14] Balance capacity was interpreted as the ability to achieve, maintain and restore the state of balance during various circumstances.[15] Balance capacity related outcome assessments of current studies are generally based on clinical tests. These reliable and valid clinical tests are widely used since they are time efficient, cost effective, and easy to administer, such as Berg Balance Scale (BBS), Time Up and Go Test (TUGT), Single Leg Stance Test (SLST).

A recent Cochrane systematic review has given the certainty of evidence that exercise programs that involved balance and functional training would reduce falls in older patients living in the community compared to inactive control groups.[16] Many recent systematic reviews have also demonstrated that exercise intervention is an effective treatment to improve balance and reduce fall rates in the elderly.[17-19] It is clear that exercise intervention could improve postural stability, balance function, and thus decrease fall risk and rate in old adults.[16,20] Exercise intervention was considered as a core element for managing T2DM and has been proved to be effective to improve various factors strongly related to T2DM and its complications, such as glycemic control, abnormal blood lipids, physical frailty, functional decline, and quality of life.[21] The guideline from International Diabetes Federation (IDF) for managing older patients with T2DM recommended that older patients with T2DM should have a fall risk assessment when they visit their health care providers annually.[22] Furtherly, this guideline recommended that older T2DM patients should receive exercise interventions with special emphasis, such as endurance training, balance training, and strength training.[22]

However, only a few systematic reviews[21,23-26] were conducted to explore exercise interventions for balance capacity related outcomes among patients with diabetes. A review[26] published in 2011 had shown insufficient evidence to support the effect of balance intervention on balance outcome in DPN patients. A systematic review without data meta-analysis

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searching for eligible studies before April 2016 was undertaken to explore the effect of falls prevention programs (lower limb strengthening, balance practice, aerobic exercise, walking programs, and Tai Chi) for T2DM patients with DPN.[23] Another systematic review that search was restricted in September 2015 was conducted to investigate the effectiveness of exercise interventions for improving fall-related factor outcomes among older adults with DM,[24] including limited studies and focusing on fall risk and fall rate as primary outcomes rather than balance capacity related outcome measures. Albalawi's systematic review was conducted in the South Asian population including only 3 trials evaluating balance outcomes with narrative review.[21] Zhou et al's[25] systematic review merely included 2 trials to explore the effect of Tai Chi on 1 balance outcome (single leg stance) for T2DM patients. All the above- mentioned reviews only evaluated clinical balance tests. However, objective measures of balance control under different conditions by sophisticated biomechanical instruments should be also paid attention to.

Since some new studies are being conducted and published continuously, but as yet, there is no systematic review exploring the effect of exercise intervention on balance capacity among specific T2DM patients. The object of this systematic review is to investigate the effect of exercise intervention on balance capacity (clinical tests and laboratory tests) in patients with T2DM.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines. The patients informed consent and ethical approval were not required since this was a review of previously published articles.

Search Strategy and Study Selection

We conducted a comprehensive literature search through PubMed, EMBASE, Physiotherapy Evidence Database (PEDro), Cochrane library, Web of Science (WOS) from inception to July 2020. The literature language was limited to English. In order to search for appropriate studies, we divided the search items into 3 different constructs: exercise, type 2 diabetes, balance or postural stability. The following items combinations were used for searching strategies: (diabetes mellitus, type 2 OR Diabetes Mellitus, Noninsulin-Dependent OR Diabetes Mellitus, Noninsulin Dependent OR Diabetes Mellitus, Ketosis-Resistance OR Diabetes Mellitus, Ketosis Resistance OR Diabetes Mellitus, Non Insulin Dependent OR Diabetes Mellitus, Non-Insulin-Dependent OR Diabetes Mellitus, Slow Onset OR Diabetes Mellitus, Slow-Onset OR Diabetes Mellitus, Maturity-Onset OR Diabetes Mellitus, Maturity Onset OR Diabetes Mellitus, Type II OR Type 2 Diabetes Mellitus OR Type 2 Diabetes OR Diabetes, Type 2 OR NIDDM OR MODY) AND (exercise OR plyometric exercise OR exercise movement techniques OR exercise therapy OR resistance training OR muscle stretching exercise OR high-intensity interval training OR physical therapy modalities OR strength OR balance training OR training OR rehabilitation OR aerobic) AND (postural balance OR balance OR postural OR postural control OR postural sway OR postural stability OR equilibrium OR center of pressure OR center of pressure OR COP OR force plate OR fall). All researches were restricted to human subjects. The search strategies were modified to fit in other electronic databases. All references of the included literatures were also hand screened.

Eligibility Criteria

Studies which met the following criteria were considered: (1) target population: patients with type 2 diabetes mellitus, mean age $\geq$ 50 years and at least 90% participants in the studies were diagnosed as type 2 diabetes mellitus; (2) interventions: any type of exercise training including strengthening exercise, balance training, aerobic exercise, Tai Chi, yoga, Qigong, or any combination of these exercises; (3) comparisons: exercise versus non-treatment/waitlist/standard care/health education/sham exercise; (4) outcomes: balance and/or postural stability including Berg Balance Scale, Time UP and Go Test, One Leg Standing Test, Functional Reach Test, fall efficacy and force platform related assessment (center of mass/center of pressure displacements/sway); (5) study designs: randomized controlled trials or quasi-experimental trials. Researches which did not meet the above inclusion criteria were excluded.

Data Extraction

Two reviewers screened the titles and abstracts for including literatures independently to exclude obvious irrelevant studies. Then they would read over the full text to identify those articles met the selection criteria. The detailed information was extracted from eligible studies, including authors, experiment locations, study design, participants characteristics (sample size, age, and disease duration), experiment group intervention, control group intervention, outcome measurements, drop-out, and adverse events. If necessary, the original authors were contacted through e-mail for additional data. All disagreements were resolved by consulting with a third reviewer.

Assessment of Risk of Bias and Quality of Evidence

We used the Physiotherapy Evidence Database (PEDro) scale to assess the methodological quality of those included studies. PEDro scale contained 11 items, including random allocation; concealed allocation; baseline comparability; blinding subjects; blinding therapists; blinding assessors;

adequate follow-up; intention-to-treat analysis; between-group comparisons; point estimates; and variability. A maximum score of PEDro scale was 10 points, 6 to 10 points was categorized as high quality; 4 to 5 points was categorized as moderate quality; <4 points was poor quality. We referred to the PEDro scores in the database, and 2 reviewers would assess the studies independently when the PEDro score was not available in the database. All disagreements were resolved by consulting with a third reviewer.

Statistical Analysis

Review Manager (RevMan 5.3, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) software was used to conduct a meta-analysis for evaluating the effect of the intervention groups in comparison to the control groups. The pre-intervention and post-intervention mean differences and standard deviations (SD) were extracted from included studies for both intervention and control groups. The effect sizes of included studies were estimated based on the net changes in outcomes evaluation since it was more sensitive to differences in pre-intervention evaluations with small sample sizes, and it was more appropriate to examine pre-post differences in intervention measurements. If a study did not report the change scores of pre-post intervention, change scores were calculated by deducting the pre-intervention score from post-intervention score. For studies reporting only means and 95% confidence intervals, the SD was calculated by dividing the confidence interval length by 3.92, then multiplied by the square root of the sample size. If the change score SD was not reported, it would be calculated by the following formula, and the correlation value was assigned as 0.5.

$$\sqrt{\text{SDbaseline}^2 + \text{SDfinal}^2 - (2 \times \text{Corr} \times \text{SDbaseline} \times \text{SDfinal})}$$

For different versions of a scale with the opposite directions, we multiply the mean values from one set of studies by −1 to ensure that all the scales point in the same direction before standardization. Meta-analysis was conducted separately for different outcome assessment tools, and a narrative review was adopted for those outcome measures reported in less than 3 trials. Heterogeneity among selected studies was indicated by the Chi-square test and I^2 value. The fixed effect model would be adopted when heterogeneity was low ($P > .1$ of Chi-square or $I^2 < 50\%$), otherwise, the random effect model would be used. Sensitivity analysis was also performed to explore the possible heterogeneity and check the stability of the pooled results. Subgroup analysis were conducted based on different participants' characteristic (such as diabetes duration, age, female portion and diabetes with/without DPN). Funnel plot asymmetry test was conducted when there are more than 10 studies in the meta-analysis.

Results

Search Selection

Figure 1 shows the detailed flow chart of studies selecting with 2361 studies. Fourteen studies were included after removing duplicates and screening of the titles, abstracts and full text for appropriate subjects, assessment, outcome. Ten of them would be included in quantitative synthesis.

Study Characteristics

Table 1 displays the characteristics of the 14 included researches.[27-40] Among these 14 studies, 3 were quasi-experimental trials[28,30,37] and the others were RCTs.[27,29,31-36,38-40] 4 trials[28,30,31,33] were conducted in China, 3 trials were conducted in USA[29,35,38] and Korea[34,36,37] respectively, 1 trial each was conducted in Singapore,[27] Kingdom of Saudi Arabia,[32] Switzerland,[39] and Australia.[40] The included studies involved 883 participants with a total attrition of 93. The sample size of the included studies ranged from 18 to 143, with the mean age ranging from 54.4 to 74.29 years old. The participants were T2DM in 8 trials,[28,30,31,33,34,36,39,40] T2DM with DPN in 5 trials[27,32,35,37,38] and T2DM with chronic pain in 1 trial.[29] The average disease duration of diabetes was between 49.77 months and 17.4 years. Various types of exercise interventions were adopted in the experimental group, including strengthening, balance training, Yoga, Tai Chi, treadmill exercise, interactive training, virtual reality exercise, and combined exercise. The major exercise intervention period ranged from 8 to 16 weeks, and only 1 trial[38] designed the intervention duration for 1 year. Exercise training frequency ranged from 1 to 7 sessions per week, with the duration of a single exercise ranging from 30 min to 2 h. All the comparison groups of the included studies were usual care, health education, no treatment, waitlist and sham exercise. There were different kinds of assessment for balance function including clinical tests and laboratory tests. Clinical test contained BBS (Berg Balance Scale), TUGT (Time Up and Go Test), FRT (Functional Reach Test), SLST (Single Leg Stance Test), FAB (Fullerton Advanced Balance) scale, 8FUG (8 foot up and go), POMA (Performance-oriented mobility assessment) balance component, Crossing beams, Tandem walk score, FES-I (Falls Efficacy Scale International), FES (Falls Efficacy Scale), MFES (Modified Falls Efficacy Scale), ABC (Activities-specific Balance Confidence) scale. Laboratory tests contained average body sway velocity measured by a balance platform (Accugait; AMTI, Watertown, MA, USA),[27] SOT (Sensory Organization Test, Smart EquiTest®),[30] postural sway measured by Metitur Good Balance System (Metitur Ltd, Jyvaskyla, Finland),[32] limit of stability examined by Bio Rescue (RM Ingenierie, Rodez, France),[34] postural stability assessed by a 2-link biomechanical model, sway index (Biodex Balance System; Biodex Medical Systems, New York, USA),[39] balance index

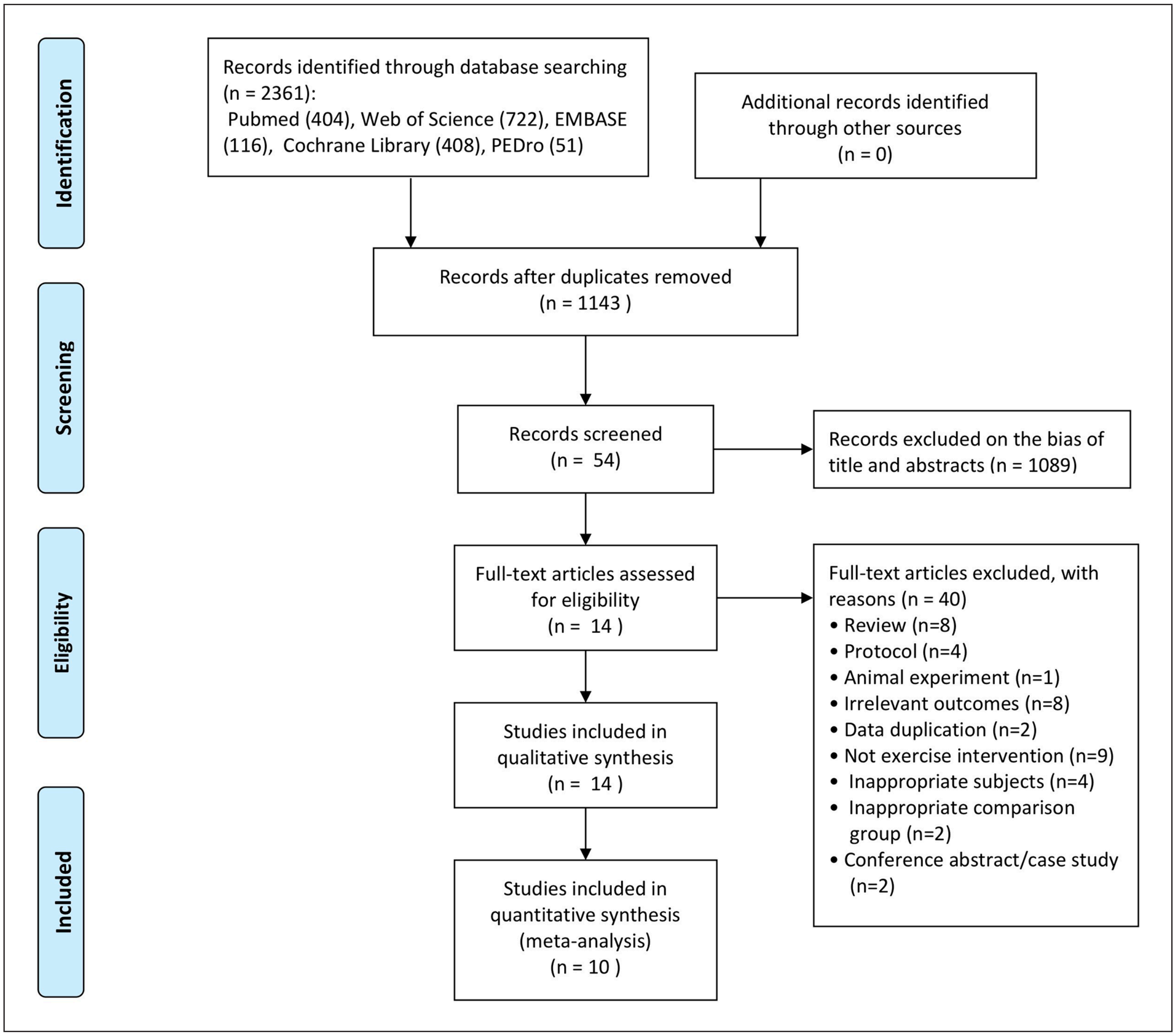

Figure 1. Flow diagram for studies selection.

(Balance System Dynamic, Chattecx, 1014, Chattanooga, TN).[40] Only 1 trial[40] reported adverse events.

Methodological Quality

Table 2 showed the methodological quality of included studies according to the PEDro scale.

The PEDro score of most included studies ranged from 5 to 8 (means moderate to high quality) except 1 study got PEDro score of 3 (means low quality). Three studies[28,30,37] were absent in random allocation since they were quasi-experimental trials. Subject blinded and Therapist blinded were absent in all studies since it was impossible to blind subjects and therapists for participants receiving exercise intervention. And only parts of included studies reported assessor blinded and intent-to- treat analysis. And drop-out rates in most studies were less than 15%.

Effect of Exercise Intervention on TUGT

Six studies[30,31,33,36,38] evaluated the effect of exercise intervention on TUGT, while 1 trial[27] did not report the post-intervention outcome assessment score but described pre-post intervention differences, and we could not get contact with the author of this trial. Although Venkataraman et al's[27] trial demonstrated significant improvements in performance in TUGT (MD=−1.14, 95% CI [−2.18, −0.10]; P=.032), the pooled results of the other 5 studies showed that exercise intervention did not improve the TUGT performance for T2DM patient (n=289; MD=−0.75; 95%CI [−1.69, 0.19]; P=.12; heterogeneity, I^2=54%, P=.07; Figure 2). However, the pooled result showed significant changes in both overall effect and heterogeneity (n=210; MD=−1.04; 95%CI [−1.77, −3.01]; P=.005; heterogeneity, I^2=52%, P=.10) after sensitivity analysis by removing Kruse et al's[38] trial.

Table. 1. Characteristics of Including Studies.

Authors	Countries	Study design	Participants; Diabetes duration	Sample size (female)	Age (years)	Intervention group	Control group	Outcome	Attrition	AE
Cai et al[28]	China	Q-E	T2DM; IG:4.93 (2.29)y CG:5.54 (3.25)y	IG:27 (14) CG:28 (17)	IG:64.54 (4.1) CG:64.51 (3.1)	Kinect-based Kaimai-style Qigong exercised, 3 sessions/week, 30 min/session, 12 weeks.	Waitlist	BBS	IG:0 CG:3	NR
Venkataraman et al[27]	Singapore	RCT	T2DM with DPN; 15.3 (10.7)y	IG:70 (34) CG:73 (46)	62	Home-based strength and balance training, 1 session/week, 8 weeks; encourage participants to perform exercise 3 to 7 sessions/week, and a median of 25 sessions during 8 weeks.	Routine care	TUGT, FRT, ABC, Body sway velocity	IG:5 CG:9	NR
Schmid et al[29]	USA	RCT	T2DM with chronic pain	IG:9 (5) CG:9 (7)	IG:56.6 (9.62) CG:53.3 (11)	Yoga intervention, 2 sessions/week, 8 weeks.	Usual care	FAB	IG:1 CG:1	NR
Ng et al[30]	China	Q-E	T2DM; IG:10.2 (8.7)y CG:10.2 (7.3)y	IG:48 (35) CG:45 (33)	IG:71.4 (7.9) CG:72.8 (6.5)	Community-based exercise and daily home exercise program focusing on ankle strengthening by applying an elastic Theraband. 60 min/session, 2 sessions/week, 10 weeks.	No treatment	SOT, TUGT, SLST	IG:2 CG:2	NR
Hsieh et al[31]	China	RCT	T2DM; IG:11.1 (7.8)y CG:13.9 (6.7)y	IG:15 (10) CG:15 (9)	IG:70.6 (4.2) CG:71.8 (4.5)	Eight resistance training exercises, the progression of exercise intensity was set at a goal of 75% 1-RM or 14 to 16 on the Borg scale from 40% to 50% 1-RM or 12 to 13 on the Borg scale, 8 to 12 repetitions/set, 3 set/day, 3 days/week, 12 weeks.	Usual care	TUGT	IG:1 CG:1	NR
Dixit et al[32]	Kingdom of Saudi Arabia	RCT	T2DM with DPN; IG:49.77 (4.72)m CG:83.71 (3.21)m	IG:36 CG:46	IG:54.40 (1.24) CG:59.45 (1.16)	Moderate-intensity treadmill exercises of 40% to 60% of heart reserve, 3 to 6 sessions/week, 8 weeks, 150 to 360 min/weeks.	Usual care	COP variables	IG:8 CG:10	NR
Xiao and Zhuang[33]	China	RCT	T2DM	IG:16 CG:16	65.5	Tai chi ball exercise, 1 to 2 h/session, 3 sessions/week, 12 weeks.	No treatment	TUGT, BBS	NR	NR
Park and Lee[34]	Korea		T2DM	IG:24 (13) CG:13 (7)	IG:71.2 (3.9) CG:69.6 (3.6)	Exercise including cardiovascular warm-up with stretching of the main muscle groups; combined exercise consisting of strengthening exercise and aerobic exercise; and the final cooling down phase for general relaxation and stretching of the trained muscle groups, 1 h/session, 3 sessions/week, 12 weeks.	No treatment	8FUG, LOS	IG:15 CG:25	NR
Grewal et al[35]	USA	RCT	T2DM with DPN; IG:17.17 ± 10.08y CG:17.40 ± 9.42y	IG:19 (11) CG:16 (8)	IG:62.58 ± 7.98 CG:64.90 ± 8.50	Sensor-based interactive exercise training tailored for people with diabetes, focusing on shifting weight and crossing virtual obstacles. 45 min/session, 2 sessions/week, 4 weeks.	Usual care	COM sway, FES-I	IG:1 CG:4	NR
Lee and Shin[36]	Korea	RCT	T2DM; IG:10.07 (7.6)y CG:9.04 (7.7)y	IG:27 (20) CG:28 (19)	IG:73.78 (4.77) CG:74.29 (5.20)	Virtual reality exercise, 50 min/session, 2 sessions/week, 10 weeks.	Health education	SLST, BBS, FRT, TUGT, MFES	IG:5 CG:4	NR
Ahn et al[37]	Korea	Q-E	T2DM with DPN; IG:12.3 (8.81)y CG:13.0 (10.03)y	IG:20 (8) CG:19 (11)	IG:66.05 (6.42) CG:62.73 (7.53)	Tai Chi for diabetes program, 60 min/session, 2 sessions/week, 12 weeks.	Usual care	SLST	IG:10 CG:10	NR
Kruse et al[38]	USA	RCT	T2DM with DPN	IG:41 (20) CG:38 (20)	IG:66.3 (10.6) CG:64.8 (9.4)	Part 1(1-3 month) included leg strengthening and balance exercises and a graduated, self-monitored walking program; part 2 (4-12 moth) included motivational telephone calls to enhance exercise.	Health education	BBS, FES, SLST, TUGT	5	NR
Allet et al[39]	Switzerland	RCT	T2DM	IG:35 CG:36	IG:63 (7.99) CG:64 (8.89)	Physiotherapeutic group training including gait and balance exercises with function orientated strengthening, 60 min/session, 2 sessions/week, 12 weeks	No treatment	POMA balance, FES-I, Crossing beam, sway index	IG:5 CG:8	NR
Tsang et al[40]	Australia	RCT	T2DM; IG:8.5y CG:9.0y	IG:18 (16) CG:20 (14)	IG:66 (8) CG:65 (8)	Supervised "Tai Chi for diabetes" exercise, a 'hybrid' form of 12 movements from Sun and Yang Tai Chi styles, 60 min/session, 2 sessions/week, 16 weeks.	Sham exercise	Balance index, SLST, Tandem walk score	IG:1 CG:0	YES

Note. IG = intervention group; CG = control group; RCT = randomized controlled trial; Q-E = Quasi-experimental trial; y = year; m = month; T2DM = type 2 diabetes mellitus; DPN = diabetic peripheral neuropath; RM = resistance maximum; BBS = Berg balance scale; TUGT = time up and go; FRT = functional reach test; ABC = activity-specific balance confidence; FAB = Fullerton advanced balance scale; SOT = sensory organization test; SLST = single leg stance test; 8FUG = 8-foot up and go; LOS = limits of stability; CoM = center of mass; COP = center of pressure; FES-I = fall efficacy scale-international; MFES = modified fall efficacy scale; FES = fall efficacy scale; POMA = Tinetti performance oriented mobility assessment; AE = adverse events; NR = not reported.

Table 2. PEDro Score for Methodological Quality Assessment of Including Studies.

Reference	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Score
Venkataraman et al[27]	1	1	0	1	0	0	0	1	1	1	1	6/10
Cai et al [28]	1	0	0	1	0	0	0	1	1	1	1	5/10
Schmid et al[29]	1	1	0	1	0	0	1	1	0	1	0	5/10
Ng et al[30]	1	0	0	1	0	0	0	1	1	1	1	5/10
Hsieh et al[31]	1	1	0	1	0	0	1	1	1	1	1	7/10
Dixit et al[32]	0	1	0	1	0	0	1	0	0	1	1	5/10
Xiao and Zhuang[33]	0	1	0	1	0	0	0	1	0	1	1	5/10
Park and Lee[34]	1	1	1	1	0	0	1	0	0	1	1	6/10
Grewal et al[35]	1	1	1	1	0	0	0	1	1	1	1	7/10
Lee and Shin[36]	1	1	0	1	0	0	0	1	0	1	1	5/10
Ahn and Song[37]	1	0	0	1	0	0	0	0	0	1	1	3/10
Kruse et al[38]	1	1	1	1	0	0	1	1	1	1	1	8/10
Allet et al[39]	1	1	1	1	0	0	1	1	1	1	1	8/10
Tsang et al[40]	1	1	1	1	0	0	0	1	1	1	1	7/10

Note. Item 1 = eligibility criteria; Item 2 = random allocation; Item 3 = concealed allocation; Item 4 = similar baseline; Item 5 = subjected blinded; Item 6 = therapists blinded; Item 7 = assessors blinded; Item 8 = <15% dropouts; Item 9 = intention-to-treat analysis; Item 10 = between-group comparison; Item 11 = point measures and variability data; 1 = described explicitly and in details; 0 = unclear, inadequately described.

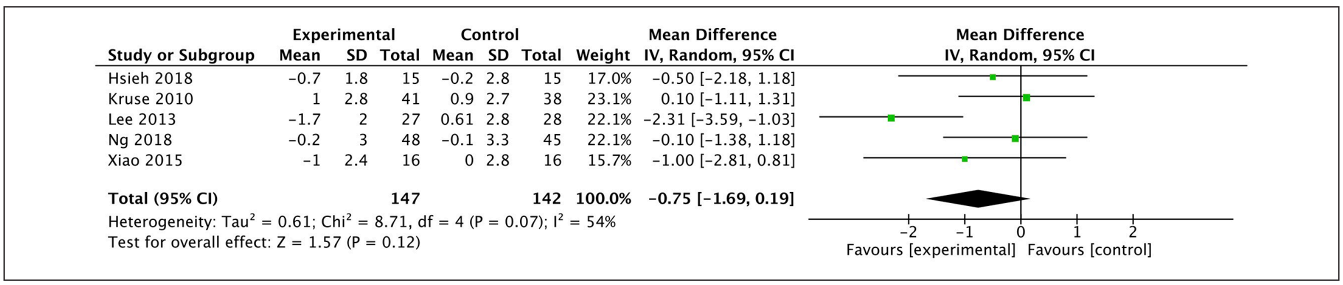

Figure 2. Forest plot of the effect of exercise intervention on TUGT.

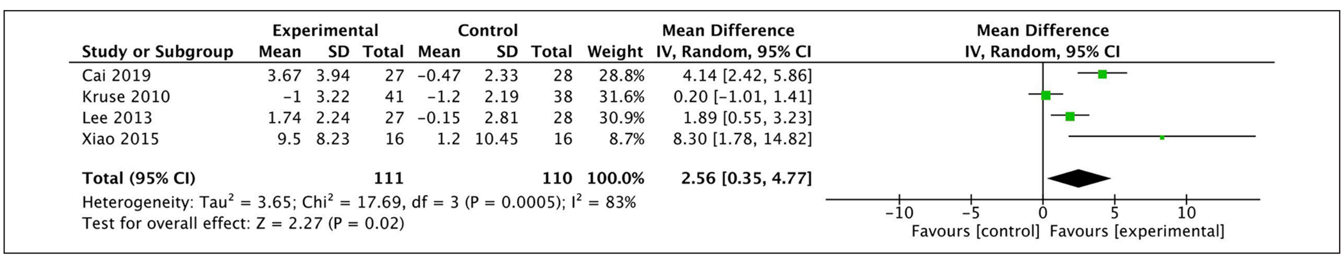

Figure 3. Forest plot of the effect of exercise intervention on BBS.

Effect of Exercise Intervention on BBS

Four studies[28,33,36,38] evaluated the effect of exercise intervention on BBS. The exercise intervention group showed significant improvement on BBS (n = 221; MD = 2.56; 95%CI [0.35, 4.77]; P = .02; heterogeneity, I^2 = 83%, P = .0005; Figure 3) in comparison with the control group (waitlist, health education, no treatment). And the pooled results appeared relatively stable after conducting sensitivity analysis by removing these studies one by one.

Effect of Exercise Intervention on SLST

A total of 5 studies[30,36-38,40] evaluated the effect of exercise intervention on SLST. Four[30,36,38,40] of them evaluated the SLST performance under the eyes-open (EO) condition, 3[37,38,40] evaluated the SLST performance under the eyes-close (EC) condition. The pooled result showed that exercise intervention group could significantly improve SLST performance under the EO condition (n = 264; MD = 3.63; 95%CI [1.79, 5.47]; P = .0001; heterogeneity, I^2 = 0%, P = .89; Figure 4) and

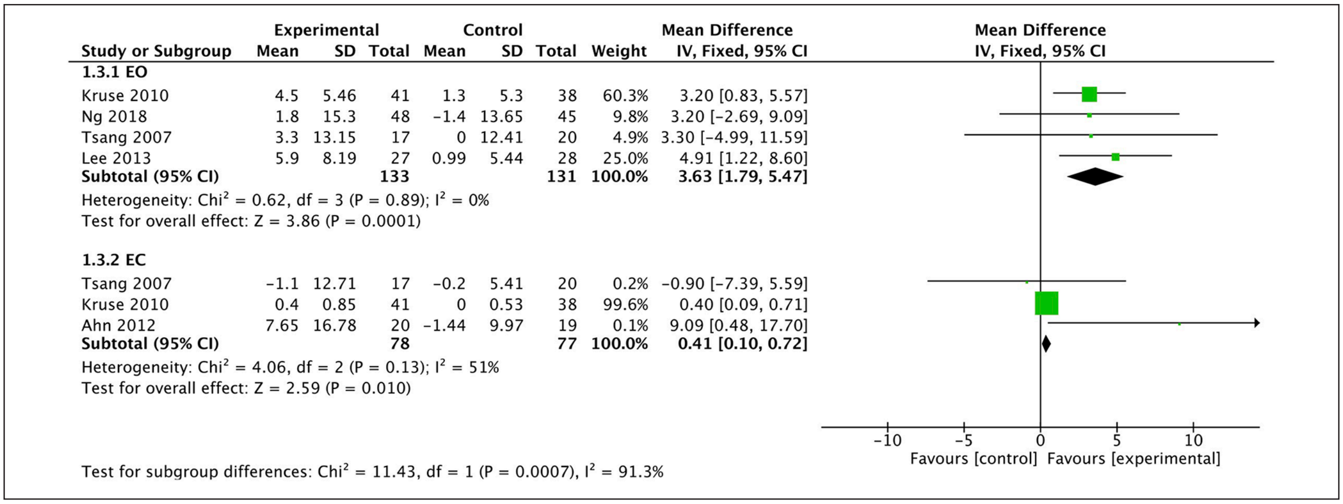

Figure 4. Forest plot of the effect of exercise intervention on SLST under EO and EC conditions.

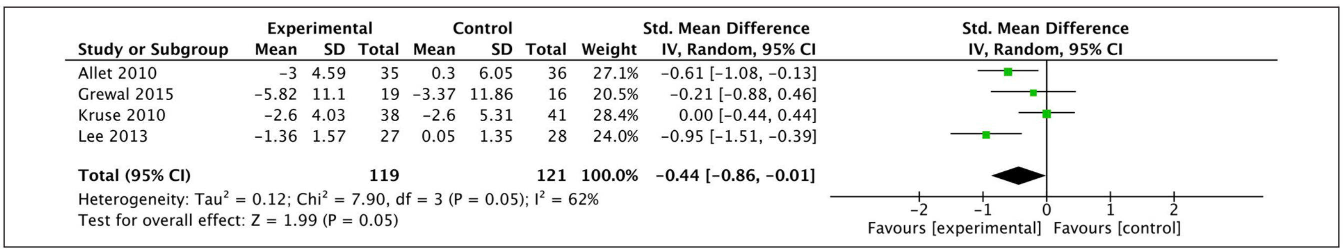

Figure 5. Forest plot of the effect of exercise intervention on fall efficacy.

EC condition (n=155; MD=0.41; 95%CI [0.10, 0.72]; P=.01; heterogeneity, I^2=51%, P=.13; Figure 4). The sensitivity analysis showed no significant changes in the mean difference and heterogeneity for SLST (EC) after excluding Ahn and Song's[37] study (PEDro score=3).

Effect of Exercise Intervention on Fall Efficacy

Five studies[27,35,36,38,39] evaluated the effect of exercise intervention on fall efficacy, 2 trials[35,39] using FES-I that high scores were associated with low falls efficacy, 1 trial each using MFES,[36] FES,[38] ABC[27] that high score were associated with high falls efficacy. While 1 trial[27] only described pre-post intervention differences, the result showed that exercise intervention could improve ABC scores (MD=5.50, 95% CI [1.31, 9.68]; P=.01). The pooled result of the other 4 studies showed that exercise intervention could not significantly improve fall efficacy (n=240; SMD=−0.44; 95%CI [−0.86, −0.01]; P=.05; heterogeneity, I^2=62%, P=.05; Figure 5). The pooled result showed significant changes in both overall effect and heterogeneity (n=161; MD=−0.62; 95%CI [−1.00, −0.24]; P=.001; heterogeneity, I^2=29%, P=.25) after sensitivity analysis by removing Kruse et al's[38] trial.

Effect of Exercise Intervention on Other Balance Capacity Assessment Tools

Some other balance capacity assessment tools were used in including studies (Table 3). Six studies used clinical tests, such as FRT,[27,36] FAB,[29] 8FUG,[34] crossing beam,[39] POMA balance component,[39] tandem walk score.[40] Seven studies used laboratory tests by specific instruments, such as body sway velocity,[27] SOT,[30] COP variables[32] under EO/EC conditions in a firm/foam surface, LOS,[34] CoM variables[35] under EO/EC conditions, balance index.[39,40]

Venkataraman et al's[27] study reported no significant differences between 2 groups in FRT (MD=0.19, 95%CI [−1.59, 1.97]; P=.836) and body sway velocity (MD=0.19, 95%CI [−0.01, 0.39]; P=.065) performances after intervention group receiving 8 weeks home-based strengthening and balance training. However, Lee and Shin's[36] study observed significant difference in FRT scores (MD=3.68, 95%CI [1.00, 6.36]; P=.007) between intervention and control groups. Schmid et al's[29] study showed no significant difference in FAB scale (MD=11.04, 95%CI [−0.91, 22.99]; P=.07) between 2 groups. Significant improvements were noted in conditions 4 (MD=5.30, 95%CI [1.91, 8.69]; P=.002), condition 5 (MD=11.10, 95%CI [6.52, 15.68]; P<.00001),

Table 3. Effect of Exercise Intervention on Other Balance Capacity Assessment Tools.

Study	Outcome measures	Intervention group post-pre mean difference (SD)	Control group post-pre mean difference (SD)	Between group mean difference (95% CI), P value	Summary of results
Venkataraman et al[27]	FRT(cm)	NR	NR	0.19 [−1.59, 1.97], P=.836	There were no significant improvements in FRT performance and body sway velocity between 2 groups.
	Body sway velocity (mm/s)	NR	NR	0.19 [−0.01, 0.39], P=.065	
Schmid et al[29]	FAB	5.84 (13.78)	−5.2 (12.02)	11.04 [−0.91, 22.99], P=.07	There were no significant improvements in FAB between 2 groups.
Ng et al[30]	SOT				Significant improvements were noted in Conditions 4 and 5 of the SOT (i.e., visual and vestibular ratios and the composite score).
	Condition 1	0.7 (4.9)	−0.6 (2.3)	1.3 [−0.24, 2.84], P=.1	
	Condition 2	−0.4 (2.2)	−0.2 (3.2)	−0.20 [−1.32, 0.92], P=.73	
	Condition 3	0.8 (3.6)	0.5 (5.1)	0.30 [−1.50, 2.10], P=.74	
	Condition 4	5.4 (8.6)	0.1 (8.1)	5.30 [1.91, 8.69], P=0.002	
	Condition 5	10.9 (12.9)	−0.2 (9.5)	11.10 [6.52, 15.68], P<.00001	
	Condition 6	5.3 (15.1)	0.8 (11.0)	4.50 [−0.85, 9.85], P=.1	
	Composite score	4.6 (6.6)	0.1 (4.9)	4.50 [2.15, 6.85], P=.002	
	Somatosensory ratio	−0.01 (0.1)	0.004 (0.04)	−0.01 [−0.04, 0.02], P=.37	
	Visual ratio	0.1 (0.1)	0.006 (0.08)	0.09 [0.06, 0.13], P<.00001	
	Vestibular ratio	0.1 (0.1)	0.002 (0.1)	0.10 [0.06, 0.14], P<.00001	
Dixit et al[32]	COP variables				In the EO condition, there were significant differences observed in the comparison of sway velocity along the x-axis and VM.
	EO				
	along x-axis (mm/s)	−0.11 (1.59)	0.86 (1.61)	−0.97 [−1.76, −0.18], P=.02	
	along y-axis (mm/s)	0.07 (1.17)	0.06 (1.16)	0.01 [−0.57, 0.59], P=.97	In the ECF condition, there were significant differences observed in the comparison of sway velocity along the x-axis
	VM (mm^2/s)	11.12 (1.82)	15.93 (1.8)	−4.81 [−5.70, −3.92], P<.00001	
	AP displacement (mm/s)	−0.1 (1.28)	−0.16 (1.24)	0.06 [−0.56, 0.68], P=.85	
	ML displacement (mm/s)	0.04 (1.23)	−0.08 (1.24)	0.12 [−0.49, 0.73], P=.7	
	EC				
	along x-axis (mm/s)	−2.4 (1.58)	−2.05 (1.57)	−0.35 [−1.13, 0.43], P=.38	
	along y-axis (mm/s)	0.05 (1.23)	0.07 (1.18)	−0.02 [−0.62, 0.58], P=.95	
	VM (mm^2/s)	0.23 (1.53)	0.18 (1.44)	0.05 [−0.69, 0.79], P=.89	
	AP displacement (mm/s)	0 (1.31)	−0.15 (1.32)	0.15 [−0.50, 0.80], P=.65	
	ML displacement (mm/s)	4.04 (1.62)	3.73 (1.55)	0.31 [−0.48, 1.10], P=.44	
	EOF				
	along x-axis (mm/s)	−0.14 (1.21)	0 (1.23)	−0.14 [−0.74, 0.46], P=.65	
	along y-axis (mm/s)	0.06 (1.19)	−0.08 (1.17)	0.14 [−0.44, 0.72], P=.64	
	VM (mm^2/s)	0.05 (1.35)	−0.13 (1.36)	0.18 [−0.49, 0.85], P=.60	
	AP displacement (mm/s)	−0.04 (1.35)	−0.03 (1.31)	−0.01 [−0.67, 0.65], P=.98	
	ML displacement (mm/s)	0.28 (1.47)	0.11 (1.55)	0.17 [−0.57, 0.91], P=.65	
	ECF				
	along x-axis (mm/s)	5.92 (1.59)	6.81 (1.49)	−0.89 [−1.65, −0.13], P=.02	
	along y-axis (mm/s)	0.12 (1.20)	0.11 (1.22)	0.01 [−0.59, 0.61], P=.97	
	VM (mm^2/s)	0.21 (1.35)	0.66 (1.37)	−0.45 [−1.12, 0.22], P=.12	
	AP displacement (mm/s)	−0.15 (1.34)	−0.26 (1.47)	0.11 [−0.58, 0.80], P=.75	
	ML displacement (mm/s)	0.04 (1.56)	−0.48 (1.58)	0.52 [−0.25, 1.29], P=.19	

(continued)

Table 3. (continued)

Study	Outcome measures	Intervention group post-pre mean difference (SD)	Control group post-pre mean difference (SD)	Between group mean difference (95% CI), *P* value	Summary of results
Park and Lee[34]	LOS (mm^2)	2692 (2600.89)	128.7 (2786.9)	2563.30 [845.31, 4281.29], *P*=.003	There were significant improvements in LOS and 8FUG between 2 groups.
	8FUG (s)	−1.1 (0.72)	0.1 (1.15)	−1.20 [−1.84, −0.56], *P*=.0003	
Grewal et al[35]	EO	N=19	N=16		Compared with the control group, the patients in the exercise intervention group showed a significantly reduced CoM sway, CoM ML sway, ankle sway and hip joint sway during the balance test with open eyes.
	CoM sway, cm^2	−2.14 (2.59)	−0.17 (1.47)	−1.97 [−3.34, −0.60], *P*=.005	
	CoM AP sway, cm	−0.42 (0.9)	−0.07 (0.52)	−0.35 [−0.83, 0.13], *P*=.15	
	CoM ML sway, cm	−0.76 (0.77)	−0.03 (0.55)	−0.73 [−1.17, −0.29], *P*=.001	
	Ankle sway, $degree^2$	−1.16 (1.61)	−0.13 (0.98)	−1.03 [−1.90, −0.16], *P*=.02	
	Hip sway, $degree^2$	−1.81 (4.32)	0.24 (0.68)	−2.05 [−4.02, −0.08], *P*=.04	
	EC				
	CoM sway, cm^2	−5.09 (10.05)	−0.65 (4.05)	−4.44 [−9.38, 0.50], *P*=.08	
	CoM AP sway, cm	−0.79 (1.59)	−0.02 (1)	−0.77 [−1.64, 0.10], *P*=.08	
	CoM ML sway, cm	−1 (1.17)	−0.41 (1.07)	−0.59 [−1.33, 0.15], *P*=.12	
	Ankle sway, $degree^2$	−1.77 (3.3)	−0.79 (3.14)	−0.98 [−3.12, 1.16], *P*=.37	
	Hip sway, $degree^2$	−1.81 (3.77)	−0.01 (2.04)	−1.80 [−3.77, 0.17], *P*=.07	
Lee and Shin[36]	FRT (cm)	4.28 (6.6)	0.6 (2.66)	3.68 [1.00, 6.36], *P*=.007	Statistically significant differences were observed for the FRT scores on the pre- and post-tests between 2 groups.
Allet et al[39]	Crossing beam (s)	−2.68 (4.89)	0.97 (4.68)	−3.65 [−5.88, −1.42], *P*=.001	Crossing beam, POMA balance and Biodex sway index showed significant between-group differences in favor of the intervention group.
	POMA balance	1.4 (1.5)	−0.5 (1.63)	1.90 [1.17, 2.63]], *P*<.00001	
	Biodex level 6 (SI)	−2.23 (2.25)	−0.01 (2.78)	−2.22 [−3.39, −1.05], *P*=.0002	
	Biodex level 8 (SI)	−1.35 (1.89)	0.14 (1.98)	−1.49 [−2.39, −0.59], *P*=.01	
Tsang et al[40]	Tandem walk score	−1 (7.73)	−1.3 (6.25)	0.30 [−4.28, 4.88], *P*=.9	No significant changes between groups were observed in the tandem walk score and balance index.
	Balance index	−3.8 (23.1)	−7.4 (22.2)	3.60 [−11.07, 18.27], *P*=.63	

Note. SD=standard deviation; CI=confidence interval; FRT=functional reach test; FAB=Fullerton advanced balance scale; SOT=sensory organization test; Condition 1=eyes open with fixed support surface; Condition 2=eyes closed with fixed support surface; Condition 3=sway-referenced vision with fixed support surface; Condition 4=eyes open with sway-referenced support surface; Condition 5=eyes closed with sway- referenced support surface; Condition 6=sway-referenced vision with sway-referenced support surface; COP=center of pressure; EO=eyes open; EC=eyes closed; EOF=eyes open on a foam surface; ECF=eyes closed on a foam surface; VM=velocity moment; AP=anterior-posterior; ML=medial-lateral; LOS=limits of stability; 8FUG=8-foot up and go; CoM=center of mass; POMA=Tinetti performance oriented mobility assessment; SI=sway index.

visual ratio (MD=0.09, 95%CI [0.06, 0.13]; $P<.00001$), vestibular ratio (MD=0.10, 95%CI [0.06, 0.14]; $P<.00001$) and the composite score (MD=4.50, 95%CI [2.15, 6.85]; $P=.002$) of the SOT between 2 groups in Ng et al's[30] trial. In Dixit et al's[32] study, there were significant differences observed in the comparison of COP sway velocity along the x-axis (MD=−0.97, 95%CI [−1.76, −0.18]; $P=.02$) and VM (MD=−4.81, 95%CI [−5.70, −3.92]; $P<.00001$) under the EO condition, sway velocity along the x-axis (MD=−0.89, 95%CI [−1.65, −0.13]; $P=.02$) under the ECF condition between 2 groups. There were significant between-group differences in LOS (MD=2563.30, 95%CI [845.31, 4281.29]; $P=.003$) and 8FUG (MD=−1.20, 95%CI [−1.84, −0.56]; $P=.0003$) of Park and Lee's[34] study. Compared with the control group, the patients in the exercise intervention group showed a significantly reduced CoM sway (MD=−1.97, 95%CI [−3.34, −0.60]; $P=.005$), CoM ML sway (MD=−0.73, 95%CI [−1.17, −0.29]; $P=.001$), ankle sway (MD=−1.03, 95%CI [−1.90, −0.16]; $P=.02$) and hip joint sway (MD=−2.05, 95%CI [−4.02, −0.08]; $P=.04$) during the balance test with open eyes in Grewal et al's[35] study. Allet et al's[39] study demonstrated significant between-group differences in favor of the intervention group in comparison of Crossing beam (MD=−3.65, 95%CI [−5.88, −1.42]; $P=.001$), POMA balance (MD=1.90, 95%CI [1.17, 2.63]; $P<.00001$) and Biodex sway index (level 6: MD=−2.22, 95%CI [−3.39, −1.05]; $P=.0002$; level 8: MD=−1.49, 95%CI [−2.39, −0.59]; $P=.01$). No significant changes between groups were observed in the tandem walk score (MD=0.30, 95%CI [−4.28, 4.88]; $P=.9$) and balance index (MD=3.60, 95%CI [−11.07, 18.27]; $P=.63$) of Tsang et al's[40] study.

Subgroup Analysis

Subgroup analysis for the various outcomes based on different types of participants' characteristic (Table 4). Participants of age larger than 70 years seemed to have better performance in OLST (EO) and fall efficacy. Participants of diabetes duration more than 10 years seemed have better performance in OLST (EO/EC). We also found that participants without DPN had better performance in BBS, OLST (EO) and FE than those with DPN.

Adverse Events

Tsang et al's[40] trial reported an adverse event. One subject with pre-existing spinal stenosis in the Tai Chi group found the exercise intolerable secondary to pain and fatigue when attending the first session.

Discussion

This systematic review and meta-analysis were conducted to assess the effect of exercise intervention on balance capacity among T2DM patients. The pooled results suggest that exercise intervention could improve balance capacity, significant differences were found on several clinical balance tests (BBS, SLST) and laboratory balance tests (SOT, COP/CoM variables, LOS) compared with the control group. The effect of exercise intervention on fall efficacy was not significant compared with the control group, which turned to be significant after conducting sensitivity analysis. The sensitivity analysis of TUGT measurements showed that the significant differences were restricted to T2DM patients without DPN in favor of the exercise intervention group. To our knowledge, the present meta-analysis was the first one to evaluate exercise intervention in balance capacity containing clinical tests and laboratory tests among T2DM patients. The main results of this review are of great importance for those T2DM patients with various degrees of balance dysfunction. Exercise intervention as a safe and convenient complementary method could help T2DM patients to get favorable outcomes.

In our review, the intervention group adopted various exercise interventions with different types, frequency, and duration. Most of the exercise types were strengthening, balance training, gait training, Tai Chi, and combined exercise. Most of the exercise treatment duration ranged from 4 to 16 weeks. How these various exercise treatments could improve the balance performance of T2DM patients remains unclear. Since balance dysfunction is a common concern in T2DM patients leading to higher fall risk and rate, it is extremely important to identify effective exercise-based treatments to improve balance capacity of T2DM patients. What is more, better balance capacity was considered as the fundamental requirements to accomplish daily life, work and leisure activities independently. Balance function maintaining involved multi-system complex interactions including sensory system (somatosensory, vestibular, visual components), motor system (adequate muscle strength, joint range of motion, flexibility) and central nervous system (feedforward, feedback, coordination, integration). Balance control contains 3 components: static posture maintenance, stability with voluntary movements, and reaction to external disturbance.[15] The exercise interventions of eligible studies including muscular strengthening, balance challenge training and weight shifting were beneficial for static and dynamic balance. And previous research concluded that T2DM patients demonstrated lower exercise capacity and unstable dynamic balance compared with health controls.[41] A systematic review showed the elderly who underwent physical exercise with improvements in static/dynamic balance, fall efficacy and physical performance compared to controls.[17] Another review also showed the effectiveness of the exercise intervention on balance performance compared with the control group, and the multi-component exercise intervention composing of balance, strength and endurance training could be the best stratagem for improving balance performance and rate of falls in old adults.[42] In line with the results of the exercise intervention for older adults, this review reached a similar conclusion. At the same time, previous research[43] showed

Table 4. Subgroup Analysis for the Effect of Exercise Intervention on Balance Capacity.

Outcome	Subgroup	Studies	Participants	Statistical method	Effect estimate
TUGT	DM duration ≥10 years	3	178	Mean difference (IV, Random, 95% CI)	−1 [−2.43, 0.43]
	DM duration <10 years	0	0	Mean difference (IV, Random, 95% CI)	0
	Age ≥70 years	3	178	Mean difference (IV, Random, 95% CI)	−1 [−2.43, 0.43]
	Age < 70 years	2	111	Mean difference (IV, Random, 95% CI)	−0.24 [−1.25, 0.77]
	Female portion ≥70%	2	148	Mean difference (IV, Random, 95% CI)	−1.21 [−3.37, 0.96]
	Female portion <70%	2	108	Mean difference (IV, Random, 95% CI)	−0.1 [−1.09, 0.88]
	DM with DPN	1	41	Mean difference (IV, Random, 95% CI)	0.1 [−1.11, 1.31]
	DM without DPN	4	210	Mean difference (IV, Random, 95% CI)	−1.01 [−2.08, 0.07]
BBS	DM duration ≥10 years	1	55	Mean difference (IV, Random, 95% CI)	1.89 [0.55, 3.23]
	DM duration <10 years	1	55	Mean difference (IV, Random, 95% CI)	4.14 [2.42, 5.86]
	Age ≥70 years	1	55	Mean difference (IV, Random, 95% CI)	1.89 [0.55, 3.23]
	Age <70 years	3	166	Mean difference (IV, Random, 95% CI)	3.28 [−0.45, 7.00]
	Female portion ≥70%	1	55	Mean difference (IV, Random, 95% CI)	1.89 [0.55, 3.23]
	Female portion <70%	2	134	Mean difference (IV, Random, 95% CI)	2.12 [−1.74, 5.98]
	DM with DPN	1	79	Mean difference (IV, Random, 95% CI)	0.2 [−1.01, 1.41]
	DM without DPN	3	142	Mean difference (IV, Random, 95% CI)	3.54 [1.14, 5.94]
OLST (EO)	DM duration ≥10 years	2	148	Mean difference (IV, Fixed, 95% CI)	4.43 [1.30, 7.55]
	DM duration <10 years	1	37	Mean difference (IV, Fixed, 95% CI)	−0.9 [−7.39, 5.59]
	Age ≥70 years	2	148	Mean difference (IV, Fixed, 95% CI)	4.43 [1.30, 7.55]
	Age <70 years	2	116	Mean difference (IV, Fixed, 95% CI)	0.4 [0.09, 0.71]
	Female portion ≥70%	2	148	Mean difference (IV, Fixed, 95% CI)	4.43 [1.30, 7.55]
	Female portion <70%	2	116	Mean difference (IV, Fixed, 95% CI)	0.4 [0.09, 0.71]
	DM with DPN	1	79	Mean difference (IV, Fixed, 95% CI)	0.4 [0.09, 0.71]
	DM without DPN	3	185	Mean difference (IV, Fixed, 95% CI)	4.29 [1.36, 7.21]
OLST (EC)	DM duration ≥10 years	1	39	Mean difference (IV, Fixed, 95% CI)	9.09 [0.48, 17.7]
	DM duration <10 years	1	37	Mean difference (IV, Fixed, 95% CI)	−0.9 [−7.39, 5.59]
	Age ≥70 years	0	0	Mean difference (IV, Fixed, 95% CI)	0
	Age <70 years	3	165	Mean difference (IV, Fixed, 95% CI)	0.41 [0.1, 0.72]
	Female portion ≥70%	1	37	Mean difference (IV, Random, 95% CI)	3.3 [−4.99, 11.59]
	Female portion <70%	2	118	Mean difference (IV, Random, 95% CI)	3.64 [−4.6, 11.87]
	DM with DPN	2	118	Mean difference (IV, Random, 95% CI)	3.64 [−4.6, 11.87]
	DM without DPN	1	37	Mean difference (IV, Random, 95% CI)	3.3 [−4.99, 11.59]
FE	DM duration ≥10 years	2	90	Std. Mean difference (IV, Fixed, 95% CI)	−0.64 [−1.07, −0.22]
	DM duration <10 years	0	0	Std. Mean difference (IV, Fixed, 95% CI)	0
	Age ≥70 years	1	55	Std. Mean difference (IV, Fixed, 95% CI)	−0.75 [−1.11, −0.39]
	Age < 70 years	3	185	Std. Mean difference (IV, Fixed, 95% CI)	−0.27 [−0.56, 0.02]
	Female portion ≥70%	1	55	Std. Mean difference (IV, Fixed, 95% CI)	−0.75 [−1.11, −0.39]
	Female portion <70%	2	114	Std. Mean difference (IV, Fixed, 95% CI)	−0.06 [−0.43, 0.3]
	DM with DPN	2	114	Std. Mean difference (IV, Fixed, 95% CI)	−0.06 [−0.43, 0.3]
	DM without DPN	2	126	Std. Mean difference (IV, Fixed, 95% CI)	−0.75 [−1.11, −0.39]

Note. DM = diabetes mellitus; DPN = diabetic peripheral neuropath; TUGT = time up and go; BBS = Berg balance scale; OLST = one leg standing test; EO = eye open; EC = eye closed; FE = fall efficacy; CI = confidence interval.

that the participants resulted in increased nerve conduction velocity and less deterioration after receiving exercise treatment, which might explain the underlying physiological reasons for the balance outcome improvement. Furthermore, various exercise interventions may result in the modulation of the sensory weighing hypothesis, which states that the postural control system is able to reweight sensory inputs to optimize stance in altered sensory environment.[32,44] The exercise could also have led to a modulation of central system set which is defined as certain postural muscles which would be selected in advance for their ability to contribute.[32,44] It is hypothesized that various types of exercise could induce moderating effects on both central nervous system and neuromuscular adaptations like synchronized recruitment of motor units, improved motor unit activation, and greater muscle force production peripherally.[32,44]

In our review, the pooled estimates of TUGT showed no significant improvements in the exercise intervention group, which was inconsistent with a previous study.[21] After conducting sensitivity analysis by removing 1 study which participants were T2DM with DPN, the pooled result of the other studies which participants were only T2DM revealed significant improvements in TUGT and heterogeneity. On this basis, it seems that the effect of exercise intervention on TUGT might be better in T2DM patients than T2DM patients with DPN. However, several recent trials[27,45,46] concluded that exercise interventions (sensorimotor training, strength and balance training, video game-base exercise) exerted positive differences on TUGT performance in T2DM patients with DPN. This reminds the future analysis could conduct subgroup analysis based on different participants (T2DM with or without DPN) if there are enough studies. Consistent with a previous review,[47] various exercise interventions had a significant effect in improving BBS and posture stability in diabetes patients. A recent systematic review[25] showed that Tai Chi did not exert an impact on balance (single leg stance test), but it just pooled data from 2 studies. On the contrary, our review found that exercise intervention could improve SLST performance significantly under both eyes-open and eyes-closed conditions with low heterogeneity. In line with this systematic review and meta-analysis, another review[23] provided preliminary evidence that T2DM with DPN patients could improve their balance capacity (clinical and laboratory tests) after a multicomponent program.

Fall efficacy or balance confidence, which defined as a person's belief of their ability to maintain balance, were known to affect the quality of life and physical activities of older adults with T2DM.[48,49] Fear of falling, lower limb strength and physical performance were more influenced when the balance function decreased.[48] A comprehensive treatment for increasing T2DM patients balance capacity should include assessment of balance performance and balance confidence. The pooled results of our review demonstrated that exercise intervention group had no significant improvements of fall efficacy compared with the control group. However, the pooled results showed significant changes in both overall effect and heterogeneity after sensitivity analysis by removing Kruse's trial. Consistent with our results, it showed better fall efficacy outcomes in the exercise intervention group compared to controls, but the differences were not significant.[17] The reason might be that the exercise intervention duration of the eligible studies was relatively too short to cause significant changes in fall efficacy.

In addition to common clinical balance tests, our review also summarized many laboratory tests using different kinds of instruments. Usually, clinical balance tests have not been validated for T2DM patients and could not explore all the symptoms of balance capacity.[50] These clinical balance tests are better described as assessment of functional performance or mobility while laboratory tests provide more objective and comprehensive data. Ventataraman's study measured static balance by average body sway velocity using a balance platform, and participants were instructed to stand on the balance platform with eyes closed for 2 min.[27] Ng et al[30] evaluated the visual, vestibular, and somatosensory functions key to postural stability maintenance were identified through a computer-based posturography device which demonstrated good test–retest reliability among community-dwelling older adults in measuring postural control. Significant improvements in visual and vestibular ratios and the composite score revealed that the participants improved to use visual and vestibular systems in postural control and balance after the exercise intervention.[30] It indicated that participants tended to avoid using the conflicting somatosensory information, relying more on the vestibular and visual information to maintain postural stability.[30] Dixit also used a balance system including a force plate to evaluate quiet static standing in 4 conditons: eyes open (EO), eyes closed (EC), and EO on foam (EOF), and EC on foam (ECF). Grewal et al[35] used validated body-worn sensor technology to collect joint kinetic data for the balance assessment. Allet et al[39] and Tsang et al[40] evaluated balance index by calculation of corresponding mathematical rules through a similar balance system. Because of adopting different balance instruments and collecting different dimensions of objective data, we could only carry out qualitative description instead of quantitative pooled analysis. We suggest that future researchers can use the same or different instruments to obtain the same dimension of outcome data under the same evaluation strategy, so that they can conduct horizontal comparison and meta-analysis to provide more convinced evidence.

For the methodological quality of these studies, it was impossible to blind the participants and therapists due to the nature of the exercise intervention. The details of concealment allocation were not descripted clearly in some studies, and a high dropout rate in some studies. In the current review, it is difficult to find the most effective exercise prescription to improve the balance function of T2DM patients since the eligible trials compared different types and doses (frequency, intensity and duration) of exercise intervention on balance capacity related outcomes. Heterogeneity of some balance capacity tests (BBS and SLST under EC condition) were identified, we should interrupt these results with caution. The limited numbers of including studies and variances between studies (participants characteristics, exercise description, outcome assessments) prevented us to explore heterogeneity by subgroup analysis. These confounding factors should be the source of such variance.

We still acknowledge several limitations in our meta-analysis. First, some relevant researches may have been missed, especially for those published in non-English languages, despite the thoroughness of search strategy. Second, this review included both RCTs and quasi-experiment studies. The participants characteristics in 14 including studies were slightly different, 8 enrolling patients with T2DM, 5 enrolling T2DM with DPN patients, and only 1 enrolling T2DM with chronic pain patients. The participants were recommended to stratify through disease severity/duration/comorbidity for future studies as the different disease situation would differ outcomes significantly. Stratifying participants could reduce the ceiling or floor effects to a certain extent, which may result in false negative results. Third, the variety of exercise interventions among including studies made it difficult to identify the optimum exercise description. Large studies are needed to establish the effect of different exercise interventions on balance capacity, and categorized exercise intervention data meta-analysis would contribute to investigate differential effect in T2DM patients with different exercise model or strategy or frequency or intensity or duration. Fourth, the objective balance capacity measured by specific instruments could not conduct meta-analysis. There is an urgent demand to investigate the effectiveness of exercise by evaluating balance capacity through specific laboratory devices, such as force plate, which could provide more comprehensive and objective outcome information. At last, we recommend researchers follow the CONSORT (Consolidated Standards of Reporting Trials) statement to conduct relevant trials.

T2DM will become more common, increasing the need for balance-related health resources.[51] This systematic review and meta-analysis of 14 studies still provides some evidence for the effect of exercise intervention to improve balance capacity among T2DM patients despite the limitation mentioned above. Further studies with high quality are required to evaluate its effectiveness.

Author Contributions

J.Q. and K.Z. contributed equally to this manuscript. J.Q. and K.Z. designed the protocol and defined the search terms. Y.C., S.G. and Y.Y. performed the search strategy. J.X. and Y.X. conducted studies review and selection. S.W. and Z.L. contributed to data extraction and literature methodology assessment. J.H. carried out the meta-analysis. J.Q. and K.Z. participated in manuscript writing. L.C. and J.Y. critically reviewed and revised the manuscript.

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