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REVIEW

A Systematic Review of the Effect of Physical Rehabilitation on Balance in People with Diabetic Peripheral Neuropathy Who are at Risk of Falling

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Background: Falls are a significant issue in people with diabetic peripheral neuropathy. Balance interventions have been broadly administered in individuals with diabetic peripheral neuropathy, but the effects on static and dynamic balance in those who are at risk of falling have not yet been comprehensively reviewed.

Objective: To provide a synthesis of the literature regarding the effectiveness of physical rehabilitation interventions to improve balance in people with diabetic peripheral neuropathy who are at risk of falling.

Methods: Four databases (PubMed, Embase, the Cochrane Central Register of Controlled Trials, Cumulated Index in Nursing and Allied Health Literature) were systematically searched from inception to July 2022. Articles meeting the eligibility criteria (ie, participants with diabetic peripheral neuropathy and at risk of falling based on validated fall balance outcome risk cut off scores; inclusion of physical rehabilitation intervention) underwent a quality assessment using the Physiotherapy Evidence Database scale. Data regarding fall risk was extracted.

Results: Sixteen studies met the eligibility criteria. Participants in six studies improved balance such that their fall risk was reduced from a moderate-high risk of falls to no or low risk of falls from pre- to post-intervention. Interventions within these six studies were variable and included balance exercise, gait training, endurance, *tai-chi* with mental imagery, proprioceptive training, aerobic training, and yoga. Participants in seven of the remaining studies showed no improvement and participants in three studies showed mixed results regarding improved balance and reduced fall risk status by post-intervention.

Conclusion: While physical rehabilitation is sufficient to improve balance in individuals with diabetic peripheral neuropathy who are at risk of falling, few interventions led to improved balance and reduced fall risk. Interventions involving intentional weight shifting, manipulation of the base of support, and displacement of the center of mass such as *tai-chi* and yoga appear to provide the most consistent results in terms of decreasing fall risk. To better understand the effectiveness of rehabilitation on balance and fall risk, future studies should examine the impact of physical interventions on prospective fall rates.

Keywords: diabetic peripheral neuropathy, fall risk, physical rehabilitation exercise interventions, balance, rehabilitation

Introduction

Diabetic peripheral neuropathy (DPN) is a common, chronic complication of diabetes that negatively impacts balance and gait.[1–3] Among neurological populations, people with peripheral neuropathy report the third highest rate of falls.[4] DPN results in loss of proprioception, cutaneous sensation, and muscle stretch reflexes in the lower limbs, which are essential for recognizing that balance has been perturbed and for triggering balance-correcting responses.[5,6] Therefore, loss of these sensory functions results in delayed balance responses, increasing the risk of falls and fall-related injuries.[7–10] People with DPN are also 15 times more likely to report injury and feel significantly less safe during standing and walking compared to healthy age-matched controls.[11] Consequently, balance training and fall prevention are essential elements of any rehabilitation program for people with DPN.

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To improve balance and reduce falls in people with DPN, several physical rehabilitative interventions have been investigated and reported beneficial effects on balance control. Such interventions include walking activities, balance training, strengthening, and aerobic exercise.[12–14] A 2011 review of physical therapy balance interventions in people with DPN concluded that interventions focusing on lower limb strengthening presented the greatest evidence for improvements in balance, with little evidence supporting the use of passive interventions such as vibrating insoles and monochromatic infrared energy.[14] However, the conclusions in this review were limited by the inclusion of lower quality studies owing to the lack of higher-level evidence available at the time. A subsequent review in 2014 determined that balance training was superior to strengthening or combined strength and endurance training with respect to improved balance in people with peripheral neuropathy.[13] However, the results of this review were not specific to DPN and included other causes of neuropathy. This is significant as the pattern of sensory loss differs depending on the cause. Therefore, the subsequent balance impairments may be different as well. A more recent review in 2017 investigating the effects of falls prevention exercises in muscle strength, balance, and fall risk factors determined that a focused multi-component intervention is optimal for the improvement of gait, balance, and function in people with DPN.[12] Nevertheless, it is essential to note that in this review, half of the studies included participants with only minimally impaired balance at the start of the intervention, as indicated by balance test scores that were above validated fall risk cut-off scores. Understanding the effectiveness of interventions in individuals across the spectrum of balance impairment severity is crucial for informing tailored treatment approaches that cater to the diverse needs of the DPN population. In DPN, demands for sensory integration and motor planning during balance challenges are increased as sensory impairments worsen. Thus, it is critical to determine whether more impaired individuals with DPN can learn to draw upon and train these compensatory centrally driven mechanisms to improve balance to the extent that fall risk is reduced. Moreover, an understanding of whether fall prevention interventions lead to a reduction in prospective falls is lacking. Since there remains insufficient data regarding long term prospective fall rates following balance rehabilitation in DPN, established fall risk cut off scores based on validated balance outcomes may be used as a proxy for fall risk.

The objective of this systematic review was to provide a synthesis of the literature regarding the effectiveness of physical rehabilitation interventions to improve balance in people with DPN who are identified as being at risk of falling. Secondarily, we aimed to determine whether any improvements in balance also led to a reduction in fall risk based on validated fall risk cut off scores and minimal clinically important differences. Ultimately, advancing our understanding of effective rehabilitation strategies for DPN-specific impairments holds the potential to mitigate fall-related morbidity and enhance overall quality of life in this population.

Materials and Methods

Search Strategies

This systematic review was registered in the PROSPERO international prospective register of systematic reviews (ID: CRD42021245702). PubMed (1809-present), Embase (embase.com, 1974-present), Cochrane Central Register of Controlled Trials (Wiley), and CINAHL (EBSCO) were searched on February 26, 2022, by a qualified librarian. All searches were performed in English. A total of 2369 articles were retrieved from the database searches. Following the removal of duplicates, 1849 articles remained. Keywords included "peripheral neuropathy" or 'peripheral nervous system disease' or 'peripheral nerve disease' or "diabetic neuropathy" AND 'fall' or 'balance' or 'postural stability' or 'postural control' or 'postural balance' or 'accidental falls' AND 'intervention' or 'rehabilitation' or 'physical therapy' or 'exercise' or 'exercise therapy' or 'exercise training' or 'program' or 'manage' or 'risk' or 'rate' or 'prevent' or 'reduce'.

Study Selection

The search strategy retrieved a total of 1605 articles from inception to July 2022 in PubMed, 671 in Embase, 162 from the Cochrane Central Register of Controlled Trials (Wiley), and 271 from CINAHL. All non-English manuscripts and duplicates were removed. Remaining articles then underwent screening and assessment for quality and eligibility.

Studies were assessed for eligibility by two independent reviewers (NA, KW) using the software Covidence. When these two reviewers were unable to reach a consensus, a third reviewer (LZ) was consulted. Studies were included in the review if they aimed to investigate the effects of a physical rehabilitation intervention on balance outcomes in people with DPN. Physical rehabilitation interventions were defined as any rehabilitation program involving active participation, such as balance activities, strengthening exercises, gait training, sensorimotor training, aerobic exercise, or tai chi. Studies involving passive (non-physical) rehabilitation, such as mental imagery, were only included if used in combination with physical rehabilitation. The outcome measures used in these studies must have had established fall risk cut-off scores. Fall risk cut-off scores were identified based upon previously published scores using balance outcome measures that are known to be valid and reliable in older adults and, if available, in people with DPN (see Table 1). Table 1 also includes the minimal clinically important difference (MCID: the minimal change in outcome scores necessary to produce a clinically meaningful improvement for a patient) for each of the included outcome measures (if available). Eligible studies included participants who were classified as being at risk for falls prior to the intervention according to the fall risk cut-off scores. In addition, study participants must have included adults with a medical diagnosis of both diabetes and sensory peripheral neuropathy of the lower limbs. Peripheral neuropathy was identified using one or more of the following criteria: reduced nerve conduction velocity, clinical neuropathy scales including the Michigan Neuropathy Screening Instrument and the modified Toronto Clinical Neuropathy Score, abnormal Semmes-Weinstein monofilaments examination, or increased vibration perception threshold.

Quality Assessment

Two independent reviewers (NA, LZ) conducted a quality assessment of all eligible studies using the PEDro scale. When these two reviewers were unable to reach a consensus, a third reviewer (KW) was consulted. The PEDro scale includes 11 criteria designed to assess clinical trials for external validity (criterion 1), internal validity (criteria 2–9), and whether there is sufficient statistical information to make results interpretable (criteria 10–11).[19] A point was awarded for each criterion if that criterion was satisfied. The total score ranges from 0 to 11. Articles with a PEDro score of less than 4 or with insufficient details regarding the intervention were excluded from the review. The PRISMA flow diagram is depicted in Figure 1.

Data Extraction

Data was manually extracted from all eligible articles by reviewer (NA). Data extracted included group means for fall-risk outcome measures with validated fall risk cut-off scores at two time points: pre-intervention and post-intervention. These fall risk outcome measures included one or more of the following measures: Berg Balance Scale, Functional Reach

Table 1 Fall Risk Cut-off Scores

<table>
<tr><th></th><th colspan="6">Fall Risk Cut-off</th><th>Sensitivity (%)</th><th>Specificity (%)</th><th>MCID</th></tr>
<tr><td>BBS[15]</td><td colspan="6">≤ 52</td><td>90[a]</td><td>76.9[a]</td><td>11.5[b]</td></tr>
<tr><td>UST[16]</td><td colspan="6">< 30 s</td><td>91[b]</td><td>75[b]</td><td>NA</td></tr>
<tr><td>FRT[15]</td><td colspan="6">≤ 31.7 cm</td><td>80[a]</td><td>65.4[a]</td><td>NA</td></tr>
<tr><td>DGI[15]</td><td colspan="6">≤ 22</td><td>90[a]</td><td>84.6[a]</td><td>1.9[b]</td></tr>
<tr><td>TUG[15]</td><td colspan="6">>10.7 s</td><td>90[a]</td><td>88.5[a]</td><td>0.8–3.4[b]</td></tr>
<tr><td rowspan="2">POMA[17]</td><td>Low</td><td colspan="3">Moderate</td><td colspan="2">High</td><td>70[b]</td><td>52[b]</td><td>NA</td></tr>
<tr><td>25–28</td><td colspan="3">19–24</td><td colspan="2">< 19</td><td></td><td></td><td></td></tr>
<tr><td rowspan="2">PPA[18]</td><td>Very Low</td><td>Low</td><td>Mild</td><td colspan="2">Moderate</td><td>Marked</td><td>75[b]</td><td>NA</td><td>NA</td></tr>
<tr><td>−2 – −1</td><td>−1 – 0</td><td>0–1</td><td colspan="2">1–2</td><td>2–3</td><td></td><td></td><td></td></tr>
</table>

Notes: [a]Determined in DPN population; [b]Determined in older adults.
Abbreviations: BBS, Berg Balance Scale; UST, Unilateral Stance Time; FRT, Functional Reach Test; DGI, Dynamic Gait Index; TUG, Timed Up and Go test; POMA, Performance Oriented Mobility Assessment; PPA, Physiological Profile Approach; MCID, minimal clinically important difference; NA, not available.

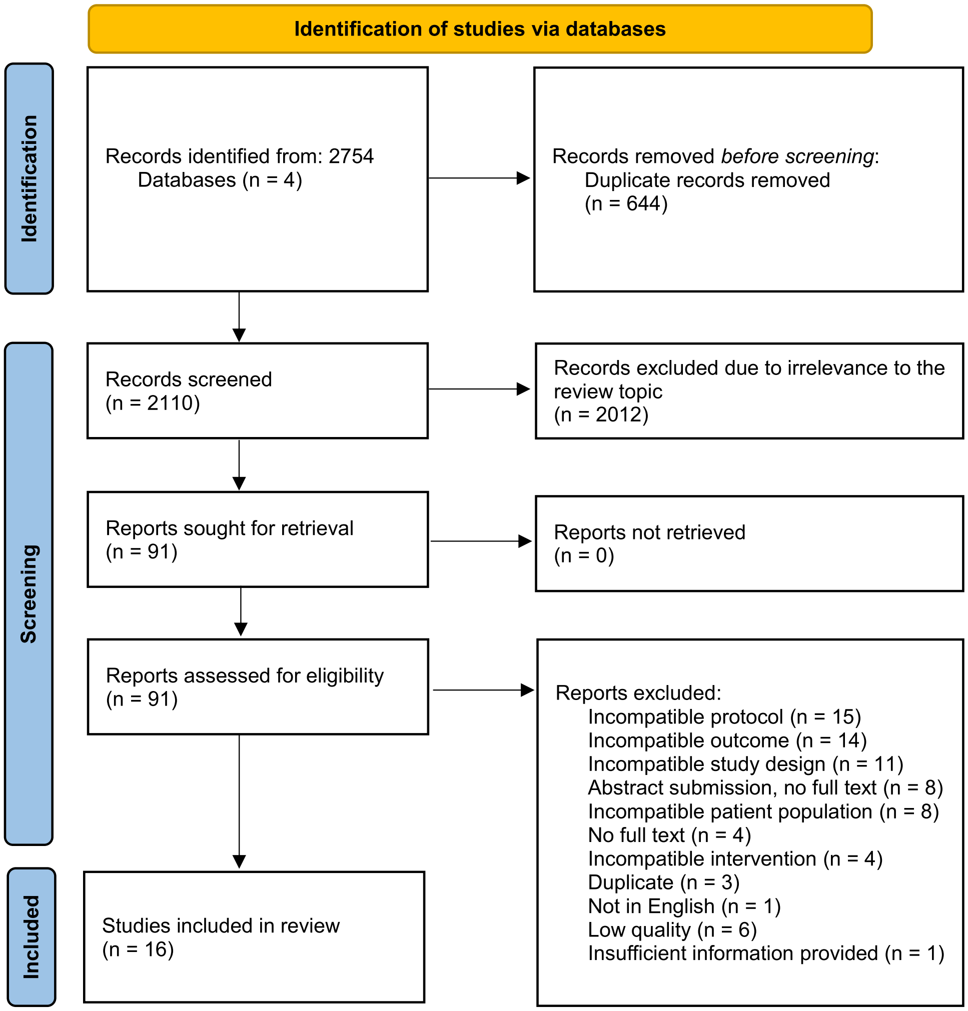

Figure 1 PRISMA flow diagram of search results and identification of eligible articles.

Test, Unilateral Stance Test, Timed Up and Go test, Dynamic Gait Index, Performance-Oriented Mobility Assessment, and Physiological Profile Approach. If any of the desired data was not provided in the article text, study investigators were contacted by (NA).

Results

Quality Assessment

The quality of the 16 included studies were assessed using the PEDro scale (Table 2). Total scores ranged from 1 to 10. Eleven of the 16 studies scored a total of 6 or above indicating moderate-to-high overall quality. All studies satisfied criterion 1 indicating good external validity. Some studies (12.5–81.3%) satisfied criteria 2–9 indicating poor-to-moderate internal validity. Most of the studies satisfied criteria 10 and 11 (87.5 and 100%, respectively) indicating sufficient statistical information to make their results interpretable. One study was excluded, despite scoring a 4 on the PEDro scale, due to insufficient details regarding the intervention.

Types of Interventions

Physical rehabilitation interventions implemented in the included studies were balance training,[21–23,25–27,29,30,34,35] sensorimotor training,[30] strength exercise,[22,23,26,29,30] gait training,[29,30] Tai Chi,[24] yoga,[33,35] aerobic training,[28] endurance training,[29] functional training,[29,30] proprioceptive training,[20,34] ball training,[32] and Frenkel exercise.[32] Four methods of

Table 2 Quality Assessment

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Abdelbasset et al, 2020[20]	1	1	1	1	0	0	1	1	1	1	1	9
Eftekhar-Sadat et al, 2015[21]	1	1	1	1	0	0	1	0	0	1	1	7
Taveggia et al, 2014[22]	1	1	1	1	1	0	1	1	1	1	1	10
Kruse et al, 2010[23]	1	1	1	1	0	0	1	1	0	1	1	8
Alsubiheen et al, 2015[24]	1	0	0	1	0	0	0	0	1	1	1	5
Song et al, 2011[25]	1	1	0	1	0	0	0	1	0	1	1	6
Richardson et al, 2001[26]	1	0	0	1	0	0	0	0	0	1	1	4
Lee et al, 2013[27]	1	1	1	1	0	0	1	1	0	1	1	8
Morrison et al, 2014[28]	1	0	0	1	0	0	0	1	1	1	1	6
Allet et al, 2010[29]	1	1	0	1	0	0	1	1	1	1	1	8
Ahmad et al, 2019[30]	1	1	0	0	0	0	0	1	1	1	1	6
Zivi et al, 2018[31]	1	1	1	1	1	0	1	1	1	1	1	10
Rojhani-Shirazi et al, 2017[32]	1	1	0	1	0	0	1	0	0	1	1	6
Willis Boslego et al, 2017[33]	1	0	0	0	0	0	0	1	1	0	1	4
Iram et al, 2021[34]	1	0	0	1	0	0	0	1	0	0	1	4
Kanjirathingal et al, 2021[35]	1	0	0	0	0	0	0	1	1	1	1	5

Note: Yes = 1, No = 0.

passive rehabilitation (transcutaneous electrical nerve stimulation,[21] whole-body vibration,[27] mental imagery,[24] visual joint movement feedback)[36] were combined with physical rehabilitation in three of the included articles. Overall, the age range for participants with DPN in these intervention studies was 46–97 years old and the duration of interventions ranged from 2–12 weeks. Methods and results of all included studies are summarized in Tables 3–5.

Effects of Physical Rehabilitation Interventions on Prospective Falls

Few physical rehabilitation studies for people with DPN assessed prospective fall rates.[23,37,38] Most studies recorded retrospective falls history over a specified period at baseline to characterize the study population, but not prospectively.[21,25,27–31] One study instructed participants to report any falls that occurred throughout the intervention to monitor adverse events.[23]

Effects of Physical Rehabilitation Interventions on Balance Outcomes

Effects on Static Balance Outcomes

The most common outcome measures of balance control used in physical rehabilitation studies in people with DPN were static outcome measures. The static balance outcome measures included postural stability measured as center of pressure (COP) sway displacement and velocity during quiet standing[27,30] or under a combination of conditions (eyes open[24,25,28,35] or closed[24,25,28,35] on firm[24,28] or foam[24,28] surface), UST with eyes open[23–25,27,30,32,34,35] and closed,[23–25,27,30,32,34,35] tandem stance,[26] and some items of the BBS.[20,21,25,27,31–34]

Most studies assessing static balance following a physical rehabilitation intervention in people with DPN found significant changes. One study[25] included only balance training in the intervention and found reductions in anteroposterior and mediolateral sway in the eyes open and eyes closed conditions, increased UST time, improvements in the static items of the BBS. Four studies using both balance training and strength exercise[22,23,26,29] found increased UST time,[23,26] improved BBS scores,[23] and increased time in tandem stance.[26] Studies using Tai Chi,[24] yoga,[33] or yogasana[35] found increased UST time,[24,35] reduced COP excursion,[35] and improved BBS scores.[33] Two studies used gait training in combination with balance training[29,30] and with sensorimotor training[30] and found reduced overall postural sway,[29,30] and increased UST time.[29,30] One study used balance training in combination with stimulation therapy[21] and found improved BBS scores. One study using only proprioceptive training[20] found improved BBS scores. One study used only aerobic training[28] and found decreased sway in the mediolateral direction, with eyes open and on a firm surface. A study

Table 3 Study Characteristics and Results

Study	Subjects	Intervention	Balance Outcomes	Results
Abdelbasset et al, 2020[20]	28 DPN; 14 intervention, 14 control	45 min, 3x per week, 2 months. Protocol: Proprioceptive training.	BBS and 6MWT	Within- and Between-Group improvements in BBS and 6MWT
Ahmad et al, 2019[30]	37 DPN	3x per week, 8 weeks. Protocol: Sensorimotor training; core exercises, balance exercises on unstable surface, and gait training.	FRT, UST eyes open and eyes closed, COP sway front-back	Significant improvements in UST EO and EC on both legs, FRT, COP range, and COP sway.
Allet et al, 2010[29]	71 DPN	60 min, 2x per week, 12 weeks. Protocol: circuit training including gait, balance, functional strength, and endurance exercises.	Dynamic balance test (participants walked as fast and as precisely as possible on a 5 m, 15 cm high, 15 cm wide beam), POMA, Biodex® sway index	Improved dynamic balance test, POMA test, and Biodex sway index.
Alsubiheen et al, 2015[24]	12 DPN, 17 controls	One hour, 2x per week, 8 weeks. Protocol: Tai Chi training combined with mental imagery.	UST, FRT, Balance platform tests (Feet apart or tandem, eyes open or eyes closed, firm or foam surface).	Within group improvements in UST, and FRT in the DPN and control groups. No significant between-group differences.
Eftekhar-Sadat et al, 2015[21]	34 DPN; 17 intervention, 17 controls	30 min, 3x per week, 10 sessions. Protocol: Intervention group: infrared and TENS, postural stability training. Controls: infrared and TENS	Fall risk index measured using the Biodex® Balance System, BBS	Improved overall stability index, and BBS in the intervention group, but no significant changes in the control group.
Iram et al, 2021[35]	38 DPN; 19 intervention, 19 controls	Intervention group: 60 min, 2x per week, 8 weeks. Protocol: proprioceptive training. Control group: 40 min, 1x per week, 8 weeks. Protocol: education.	UST, BBS, TUG	Improved UST with eyes open, but not with eyes closed, and improved BBS and TUG in the DPN group. No significant within group differences in the control group.
Kanjirathingal et al, 2021[35]	35 DPN; 11 yogasana, 10 conventional balance, 14 controls	60 min, 3x per week, 12 weeks. Protocol: Intervention groups: Group 1: yogasana, Group 2: conventional balance exercise.	UST with eyes open and closed, SEBT, COP excursion	Within-group improvements in UST with eyes open and closed, SEBT, and COP excursion in the yogasana and conventional groups. Greater improvements in the SEBT and UST with eyes open and closed in the yogasana group compared to the other groups.
Kruse et al, 2010[23]	79 DPN; 41 intervention, 38 controls	One hour, 3x per week, 12 months. Protocol: Part 1: leg strengthening, balance exercises, and a walking program. Part 2: home exercise and motivational telephone calls.	BBS, UST with eyes open and eyes closed. Assessments at baseline, 6 months, 12 months.	UST with eyes closed improved at 12 months in intervention group
Lee et al, 2013[27]	55 DPN; 19 WBV, 18 conventional, 18 control	2x per week, 6 weeks. Protocol: WBV training and 60 min per day of balance exercise. Conventional: 60 min per day balance exercise. Controls: no intervention	Postural sway, UST, BBS, FRT.	Improvements in postural sway, UST, BBS, FRT in the WBV group, compared to conventional and control.

(*Continued*)

Table 3 (Continued).

Study	Subjects	Intervention	Balance Outcomes	Results
Morrison et al, 2014[28]	16 DPN, 21 DM	3x per week, 12 weeks. Protocol: aerobic exercise for both groups consisting of treadmill walking or running, stationary cycling, and/or elliptical strider workouts	Hand and foot reaction times, PPA, mean velocity of sway in eyes open vs eyes closed and firm vs foam surface conditions, path length, and range of COP motion in the ML direction	Improved COP parameters in the eyes open/firm surface condition. Improved hand and foot reaction times.
Richardson et al, 2001[26]	20 DPN; 10 intervention, 10 controls	Daily, 3 weeks. Protocol: warm up, bipedal toe and heel raises, bipedal inversion and eversion, unipedal toe and heel raises, unipedal eversion and inversion, wall slides, unipedal balance	Tandem stance, FRT, UST	Improved tandem stance, FRT, and UST in the intervention, but not control group.
Rojhani-Shirazi et al, 2017[32]	60 DPN; 20 ball exercise intervention, 20 Frenkel exercise intervention, 20 control	55 min, 5x per week, 3 weeks. Protocol: ball training and Frenkel exercise. Controls: no intervention.	UST, BBS, SEBT	Improved within-group UST, BBS, and SEBT in both intervention groups. Between-group improvements in UST, BBS, and SEBT in all directions in both intervention groups compared to controls. The ball training group showed greater improvements in all outcomes compared to the Frankel group.
Song et al, 2011[25]	38 DPN; 19+ intervention, 19 control	60 min, 2 times per week, 8 weeks. Protocol: both groups received health education on diabetes for 50min/week for 8 weeks. The intervention group also had balance training	Postural sway, UST, BBS, FRT	Improved postural sway, UST, BBS and FRT in the intervention group.
Taveggia et al, 2014[22]	27 DPN; 13 intervention, 14 control	5x per week, 4 weeks, 2-month follow-up. Protocol: multimodal manual treatment; treadmill, strength, dynamic balance. Controls: endurance, strengthening, stretching, gait, balance.	POMA	No significant change in the POMA
Willis Boslego et al, 2017[33]	15 DPN	1 hour, 2x per week, 8 weeks. Protocol: yoga, positive affirmations, breathing, postures and relaxation.	BBS	Improved BBS scores
Zivi et al, 2018[31]	40 DPN; 21 aquatic training, 19 land training	Aquatic: 3x per week, 4 weeks. Protocol: relaxation and breath control; balance, posture control, gait exercises. Land: 5–6x per week, 4 weeks. Protocol: conventional physical and occupational therapy.	BBS, DGI	Greater improvement in DGI in the aquatic group compared to the land group. No significant differences in BBS between groups.

Abbreviations: DPN, diabetic peripheral neuropathy; BBS, Berg Balance Scale; 6MWT, 6-Minute Walk Test; FRT, Functional Reach Test; UST, Unilateral Stance Test; COP, Center of Pressure; POMA, Performance Oriented Mobility Assessment; TUG, Timed Up and Go; SEBT, Star Excursion Balance Test; WBV, Whole Body Vibration; DM, Diabetes Mellitus; PPA, Physiological Profile Assessment; ML, Mediolateral; DGI, Dynamic Gait Index.

Table 4 Studies with Improved Fall Risk Status

Study	Fall Risk Outcome	Results			Falls
		Fall Risk Pre-Intervention (mean)	Fall Risk Post-Intervention (mean)	p-value	
Allet et al, 2010[29]	POMA	Moderate risk (23)	Low risk (25)	< 0.002	History of falls recorded at baseline
Alsubiheen et al, 2015[24]	FRT	At risk (28.45 cm)	Not at risk (32.51 cm)	< 0.001	Not recorded
	UST	At risk (29.8 s)	Not at risk (48.5 s)	< 0.01	
Iram et al, 2021[34]	UST	At risk (25.9 s)	Not at risk (32.8 s)	0.001	Not recorded
	TUG	At risk (12.7 s)	Not at risk (9.05 s)	0.001	
	BBS	At risk (34.6)	Not at risk (53.3)	0.001	
Kanjirathingal et al, 2021[35]	UST	Right: At risk (17.7 s) Left: At risk (17.4 s)	Right: Not at risk (49.7 s) Left: Not at risk (50.3 s)	0.003 0.003	Not recorded
Morrison et al, 2014[28]	PPA	Mild risk (0.39)	Low risk (−0.07)	> 0.05	History of falls recorded at baseline
Willis Boslego et al, 2017[33]	BBS	At risk (49.33)	Not at risk (53)	0.009	Not recorded

Abbreviations: BBS, Berg Balance Scale; UST, unilateral stance test; FRT, functional reach test; POMA, Performance Oriented Mobility Assessment; PPA, Physiological Profile Approach; TUG, Timed Up and Go.

Table 5 Studies Without Improved Fall Risk Status

Study	Fall Risk Outcome	Results			Falls
		Fall Risk Pre-Intervention (mean)	Fall Risk Post-Intervention (mean)	p-value	
Abdelbasset et al, 2020[20]	BBS	At risk (47.5)	At risk (51.3)	0.003	Not recorded
Eftekhar-Sadat et al, 2015[21]	TUG	At risk (11.18 s)	At risk (10.97 s)	0.002	History of falls recorded at baseline
Kruse et al, 2010[23]	UST	At risk (10.1 s)	At risk (15.7 s)	0.890	Throughout the study: 9 participants in each group fell once, 7 participants in each group fell 2 or more times.
	BBS	At risk (48.1)	At risk (48.1)	0.910	
Richardson et al, 2001[26]	FRT	At risk (26.67 cm)	At risk (29.21 cm)	0.0012	Not recorded
	UST	At risk (5.4 s)	At risk (11.6 s)	0.0014	
Rojhani-Shirazi et al, 2017[32]	UST	Ball Training:			Not recorded
		Right: At risk (5.12 s) Left: At risk (3.84 s)	Right: At risk (9.22 s) Left: At risk (6.49 s)	< 0.001 < 0.001	
		Frenkel Training:			
		Right: At risk (5.54 s) Left: At risk (4.12 s)	Right: At risk (7.88 s) Left: At risk (5.41 s)	< 0.001 < 0.001	

(*Continued*)

Table 5 (Continued).

Study	Fall Risk Outcome	Results			Falls
		Fall Risk Pre-Intervention (mean)	Fall Risk Post-Intervention (mean)	p-value	
	BBS	Ball Training:			
		At risk (44.5)	At risk (47.35)	< 0.001	
		Frenkel Training:			
		At risk (42.35)	At risk (44.05)	< 0.050	
Taveggia et al, 2014[22]	POMA	High risk (9.7)	High risk (11.4)	0.900	Not recorded
Zivi et al, 2018[31]	BBS	Aquatic:			History of falls recorded at baseline
		At risk (36.0)	At risk (51.0)	<0.010	
		Conventional:			
		At risk (31.0)	At risk (41.0)	<0.010	
	DGI	Aquatic:			
		At risk (15)	At risk (21)	<0.010	
		Conventional:			
		At risk (11)	At risk (15)	<0.010	

Abbreviations: BBS, berg balance scale; UST, unilateral stance test; FRT, functional reach test; POMA, Performance Oriented Mobility Assessment; TUG, Timed Up and Go; DGI, Dynamic Gait Index.

comparing ball training and Frenkel exercise[32] found greater increase in UST time and improved BBS scores in the ball training group compared to the Frenkel exercise group.

Effects on Dynamic Balance Outcomes

Relatively few intervention studies for people with DPN have assessed dynamic balance. The dynamic balance outcome measures included in this review were the FRT,[24–27,30] PPA,[28] TUG,[34] some items of the BBS,[20,21,23,25,27,31–34] POMA,[22,29] and DGI.[31]

Most studies assessing dynamic balance following a physical rehabilitation intervention in people with DPN have reported significant changes. Studies that included only balance training[25] in the intervention found improvements in the dynamic items of the BBS and improved FRT distance. Four studies using both balance training and strength exercise[22,23,26,29] found improved POMA scores,[29] improved BBS scores,[23] and increased FRT distance.[26] Studies using Tai Chi,[24] yoga,[33] or yogasana[35] found increased FRT distance,[24] improved SEBT,[35] and improved BBS scores.[33] Two studies used gait training in combination with balance training[29,30] and with sensorimotor training[30] and found increased FRT distance[30] and increased POMA scores.[29] One study used balance training in combination with stimulation therapy[21] and found improved BBS scores. One study using only proprioceptive training[20] found improved BBS scores and 6MWT distance. A study comparing ball training and Frenkel exercise[32] found greater improvement in SEBT performance and improved BBS scores in the ball training group compared to the Frenkel exercise group. One study compared aquatic- and land-based rehabilitation[31] and found greater improvement in DGI in the aquatic group compared to land group.

One study assessing dynamic balance outcomes did not find any significant changes following the intervention (POMA).[22]

Effects of Physical Rehabilitation Interventions on Fall Risk

Fall Risk Outcome Measures

The 16 included studies utilized a combined total of seven balance outcome measures with validated fall risk cut-off scores. Nine studies included the Berg Balance Scale (BBS).[20,21,23,25,27,31–34] The BBS measures static and dynamic balance during 14 common tasks that are rated on a 5-point ordinal scale from 0 (lowest level of function) to 4 (highest level of function). The BBS has an MCID of 11.5.[39] Nine studies included unilateral stance time UST,[23–27,30,32,34,35] which measures unipedal static balance with eyes open. The UST has no known MCID. Five studies reported results from the Functional Reach Test (FRT),[24–27,30] which measures anticipatory and dynamic balance. Participants are instructed to reach forward as far as they can without taking a step and the distance from the initial to end reach position is measured. The FRT has no known MCID. Two studies reported the Performance Oriented Mobility Assessment (POMA).[22,29] The POMA, also called the Tinetti test, is a task-oriented 16 item test that measures balance and gait and is scored on a 3-point ordinal scale from 0 (high level of impairment) to 2 (independent). The POMA has no known MCID. Only one study included the Physiological Profile Assessment (PPA),[28] which is a fall risk assessment tool. The PPA includes measures of vision, peripheral sensation, muscle force, reaction time, and postural sway. The PPA has no known MCID. Only one study included the Dynamic Gait Index (DGI),[24] which assesses gait and balance while walking in the presence of external demands such as changing speeds and head turns. The DGI has an MCID of 1.9.[40] Five studies included the Timed Up and Go Test (TUG),[21,25,27,30,34] which involves timing the participant as they stand up from an armless chair, walk 3 meters, turn, walk back to the chair, and sit down. The TUG has an MCID of (0.8–3.4).[41,42]

Changes in Fall Risk

Results of the 16 included studies were examined for changes in fall risk status (ie, transitioned from being at fall risk to not at fall risk) resulting from the intervention and according to validated cut-off scores (Table 1).[20–35] We used the mean scores for each fall risk outcome at baseline and post-intervention testing since individual participant values were not always available.

Six of the 16 included studies reported improvement in fall risk status, changing from at risk of falls to not at risk of falls, following the intervention (Table 4). Within these studies, fall risk cut off scores were taken from the UST,[24,34,35] TUG,[34] BBS,[33,34] FRT,[24] PPA,[28] POMA,[29] and DGI.[31] The interventions implemented in these studies included balance, gait, functional strength, endurance, tai chi with mental imagery, proprioceptive training, yogasana, aerobic training, and yoga and relaxation. Durations of these interventions were 8[24,33] and 12[28,29,35] weeks.

Seven of the 16 studies did not report change in fall risk status by post-intervention (Table 5). Within these seven studies, fall risk cut off scores were taken from UST,[23,26,32] BBS,[20,23,31,32] FRT,[26] TUG,[21] POMA,[22] and DGI.[31] Types of interventions implemented in these studies included proprioceptive training, sensorimotor training, balance, gait, postural stability training with TENS and infrared therapy, walking, ball training, and Frenkel training. Durations of these interventions were 3,[21,26,32] 4 weeks,[22,31] 8,[20] and 12 months.[23]

Three of the 16 included studies reported conflicting results regarding whether fall risk status improved following the intervention due to different outcome measures used within each study (Table 6).[25,30] All three studies included UST and TUG,[25,27,30] with the TUG added in two of the studies.[25,27] The interventions implemented in these studies included sensorimotor, balance, core, and gait training. The durations of these interventions were 6[27] and 8 weeks.[25,30]

Table 6 Studies with Mixed Results Regarding Fall Risk Status

Study	Fall Risk Outcome	Results			Falls
		Fall Risk Pre-Intervention (mean)	Fall Risk Post-Intervention (mean)	p-value	
Ahmad et al, 2019[30]	UST*	Right: At risk (24.62 s) Left: At risk (20.97 s)	Right: Not at risk (34.66 s) Left: At risk (28.22 s)	0.003 0.043	History of falls recorded at baseline
	TUG*	At risk (10.72 s)	Not at risk (9.46 s)	< 0.001	

(*Continued*)

Table 6 (Continued).

Study	Fall Risk Outcome	Results			Falls
		Fall Risk Pre-Intervention (mean)	Fall Risk Post-Intervention (mean)	p-value	
Lee et al, 2013[27]	FRT*	WBV + Balance:			History of falls recorded at baseline
		At risk (27.89 cm)	Not at risk (32.35 cm)	0.001	
		Conventional:			
		At risk (27.77 cm)	At risk (29.91 cm)	0.010	
	UST	WBV + Balance:			
		At risk (17.64 s)	At risk (24.05 s)	0.001	
		Conventional:			
		At risk (17.99 s)	At risk (19.67 s)	0.011	
	BBS	WBV + Balance:			
		At risk (49.47)	At risk (51.37)	0.001	
		Conventional:			
		At risk (48.67)	At risk (49.28)	0.045	
	TUG	WBV + Balance:			
		At risk (13.31 s)	At risk (11.53 s)	0.001	
		Conventional:			
		At risk (13.66 s)	At risk (12.84 s)	0.034	
Song et al, 2011[25]	FRT	At risk (27.1 cm)	At risk (30.9 cm)	< 0.010	History of falls recorded at baseline
	UST	Right: At risk (5.9 s) Left: At risk (6.2 s)	Right: At risk (11.6 s) Left: At risk (9.9 s)	< 0.050 < 0.010	
	TUG*	At risk (11.8 s)	Not at risk (10.1 s)	< 0.010	

Note: *Denotes a reduction in fall risk.
Abbreviations: BBS, berg balance scale; UST, unilateral stance test; TUG, timed up and go test; FRT, functional reach test; WBV, whole body vibration.

Of the studies in this review reporting outcome scores that improved from below to above the fall risk cut off, only three reported a score increase that was greater than their respective MCID values. These three studies included the TUG and BBS. The interventions implemented in these studies included proprioceptive training,[34] sensorimotor training,[30] and balance training.[25]

Discussion

This review summarizes the results from 16 physical rehabilitation studies that included people with DPN who were at risk of falls at baseline based on established fall risk cut off scores. Overall, although physical rehabilitation interventions found improvements in balance outcomes, it is less clear whether they are reducing fall risk. None of the included studies assessed prospective fall rates following physical rehabilitation interventions in people with DPN.

Using the established fall risk cut-off scores of included balance outcome measures, only six of the 16 studies led to an improvement in fall risk status post-intervention.[24,28,29,33–35] Seven of the 16 studies failed to result in a change in fall risk status post-intervention,[20–23,26,31,32] and three studies demonstrated variability in fall risk status change.[25,27,30] The lack of change in fall risk status in most of these studies may primarily be explained by differences in balance outcome measures as well as the type and dosage of physical rehabilitation interventions of the included studies.

Balance Outcome Measures

Interestingly, five of the seven outcomes within the studies included in this review were common among studies in which a reduction in fall risk was identified (Table 4) and was not identified (Table 5). This discrepancy may be due, at least in part, to the fall risk sensitivity and specificity for each outcome and whether these values have been specifically tested in a DPN population. It may be argued that the results of Table 4 were more dependent on the specificity by which fall risk cut off scores can accurately rule out the participants who were not at risk of falls following the intervention. Of the outcomes included in the six studies resulting in a reduction in fall risk, specificity ranged from 65.4–88.5%, suggesting that there may have been up to 35% of the study participants who remained at risk of falls following the intervention. In contrast, the results of Table 5 may be more dependent on the sensitivity by which participants who remained at risk for falls could be accurately identified. Of the outcomes included in the seven studies in Table 5, the fall risk sensitivity ranged from 70–91%, suggesting that up to 30% of the study participants had improved their fall risk status. The range of fall risk specificity and sensitivity may also explain the within study discrepancy of results noted in Table 6. Moreover, only four of the seven reported outcomes have been validated for fall risk cut off scores in a population with DPN. Although UST, POMA, and PPA have been validated in an older adult population at risk of falling, specific fall risk cut off scores for DPN have not yet been established. To our knowledge, there are no studies that validate and compare the psychometric properties and sensitivity and specificity of fall risk cut off scores across balance outcome measures in people with DPN. Therefore, it is difficult to ascertain which of the outcome measures included in the studies of this review are optimal measures of fall risk in this population.

Differences in the test items included in the outcome measures included in this review should also be considered in light of the discrepancies of our results. For example, the UST and FRT are single-task tests that rely chiefly on feet in place balance strategies. On the other hand, the BBS measures a series of static and dynamic balance tasks but does not address balance while walking. Given that the conditions under which people with peripheral neuropathy most often fall include walking over irregular (67.1%) or slick (11.8%) surfaces,[43] outcome measures that include walking assessments such as the TUG, DGI, and POMA may be better options for the assessment of fall risk in people with DPN. People with peripheral neuropathy also commonly fall while turning and reaching beyond the base of support (22.5%).[43] Of the outcome measures included in this review, only the BBS, TUG, POMA, and DGI included turning assessments.

Another point of consideration is the presence of floor or ceiling effects among the reported outcome measures. Ceiling effects have been documented among older adults in the BBS,[40] UST,[44] POMA,[40] and DGI.[40] Floor effects have been documented among older adults in the TUG.[45] Therefore, in this review, relatively younger participants with less severe impairments may not be sufficiently challenged during the balance assessment tasks, resulting in a ceiling effect. In contrast, participants who were more severely impaired may have been unable to perform many of the tasks, resulting in a floor effect. To account for floor and ceiling effects, we included all fall risk assessments used in each of the studies. This allows for the consideration of other scales used in the same study which can corroborate any fall risk improvement or lack thereof. We also included outcomes with continuous measurements, such as the PPA and FRT, which avoid floor and ceiling effects. Moreover, it should be noted that even though six of the 16 included studies reported improvement in fall risk status from at risk of falls to not at risk of falls, only three of these six studies also reached MCID values.

Differences in Rehabilitation Interventions

Balance training was included in most of the included studies, but only one of these studies resulted in reduced fall risk[29] and three others reported conflicting results.[25,27,30] There are several possible explanations for the lack of fall risk reduction in these studies. First, the intensity of the intervention, either duration, frequency, or a combination of these exercise dosage parameters, may not have been sufficient to produce significant changes. The one study that resulted in reduced fall risk had a longer intervention duration than the others (ie, 12 weeks vs 6 or 8 weeks). Second, some studies only included static balance training, which may not be as effective as dynamic or walking balance interventions in reducing fall risk. Third, it is possible that balance interventions alone are not capable of reducing fall risk in individuals with DPN and that balance training needs to be combined with other related interventions. A recent meta-analysis comparing the effectiveness of different exercise interventions in reducing falls in healthy older adults[46] found that the greatest reduction in numbers of fallers occurred with exercise combinations that included four components of balance (anticipatory control, dynamic stability, functional stability limits, and reactive control) and flexibility. People with DPN typically experience somatosensory loss beginning in the distal lower limbs, resulting in reduced feedback control.[7] It is possible that multiple domains of balance need be trained as a comprehensive training protocol to effectively target the deficits caused by sensory loss and the integration of residual sensory systems.

Three studies included training that involved mindful whole-body motions (Tai Chi, yoga, and yogasana).[24,33,35] All three of these studies improved balance as well as improvements in fall risk status from at-risk to not-at-risk in all included balance assessments. These studies involved intentional weight shifting, base of support manipulation, and center of mass displacement. Such movements place a high demand on balance control and whole-body awareness, which may explain the consistent balance and fall risk improvement shown in all the included studies that involved this type of intervention. However, these results should be interpreted with caution as these three studies received lower quality assessment scores.

Two studies included gait training, both of which showed improvements in balance, however, only one resulted in reduced fall risk[29] and the other produced contradictory results.[30] Gait training was combined with strength and balance training in both studies with the addition of sensorimotor training in one of these studies.[30] In addition, the study that resulted in reduced fall risk had a longer intervention duration. Given that most falls in people with peripheral neuropathy occur while walking, it is plausible that a fall prevention program including interventions aimed at improving balance control while walking may have greater potential for reducing falls in people with DPN.[43,47]

People with DPN typically experience somatosensory loss resulting in reduced feedback control.[7] To date, all physical rehabilitation interventions in people with DPN have focused on training and exercises aimed at improving feedforward (ie, anticipatory) control. An intervention aimed at improving feedback (ie, reactive) rather than feedforward balance control may potentially have a greater impact on balance and fall risk in people with DPN. Reactive balance training has proven effective in reducing falls in other populations.[48,49] To our knowledge, no previous studies have examined the effects of a reactive balance training intervention on balance or falls in people with DPN.

The physical rehabilitation interventions included in this review were highly variable regarding the type, duration, intensity, and frequency of training. The included studies used a total of fourteen different types of physical rehabilitation interventions with durations ranging from two weeks to twelve months and frequencies of daily to twice weekly sessions. However, there were a few intervention types in common between the studies that resulted in improved fall status.

Limitations

There are several Limitations of this review that should be mentioned. First, many studies included a relatively wide age range, including middle aged and older adults, but not all controlled for age-related differences in balance control when analyzing and reporting their results. Consequentially, it was not always clear whether reduced fall risk, or lack thereof, is due to age-related or DPN-related physiological changes. Second, there was high variability in severity of DPN among participants, intervention type, intensity, frequency, and duration, as well as outcome measures and the instruments and analysis methods used to measure them, which may limit generalizability of some results. Third, it is important to note that to definitively declare that fall risk has improved would require that the individual studies complete a long-term follow-up with their participants to determine whether they have experienced any new falls. There is currently a paucity of physical rehabilitation training studies in people with peripheral neuropathy, which have prospectively followed up with their participants. In this review, we used the information available to us to infer the effects of the included interventions on fall risk. Finally, many of the interventions were conducted as a pre-post single cohort study. As a result, these studies received low PEDro scores for items concerning between group differences, blinding, and randomization. Single group design increases the risk for bias and makes it difficult to determine if any improvements in outcomes are due to the intervention or another factor that may not have been considered or controlled. Future studies should improve quality where possible by utilizing randomized controlled trial design, blinding assessors, and providing clear and detailed results.

Conclusions

Although physical rehabilitation interventions have been found to improve walking speed, strength, and other static and dynamic balance tests, the effect on fall risk and prospective fall rates remains unclear. Regarding the clinical implications of this review, the intervention types that consistently resulted in reduced fall risk were interventions such as Tai

Chi and yoga, which require intentional weight shifting, base of support manipulation, and center of mass displacement. In addition, clinicians should consider the psychometric properties of fall risk assessments, as well as the ceiling and floor effects, when deciding which clinical balance measures to use to determine whether improvements in fall risk have been achieved. Future studies should explore the long-term effects of physical rehabilitation interventions on prospective fall rates. In addition, future studies should carefully consider the properties and design of their chosen outcome measures when assessing fall risk in people with DPN.

Disclosure

The authors report no conflicts of interest in this work.

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