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REVIEW

Effectiveness of Exercise Therapy on Gait Function in Diabetic Peripheral Neuropathy Patients: A Systematic Review of Randomized Controlled Trials

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Abstract: The purpose of this study was to review the current evidence on the effectiveness of exercise therapy on gait function in patients with diabetic peripheral neuropathy. A comprehensive search of literature published between October 2010 and May 2020 was conducted using the following electronic databases; PubMed, AMED, CINAHL, ScienceDirect, Cochrane Library, PEDro and Google Scholar. Randomized control trials conducted to determine the effectiveness of exercise therapy on gait function in patients with diabetic neuropathy were included in this review. Non-English language published papers were excluded. This review was done in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Data extraction and risk of bias assessment of the studies were carried out independently by two authors. The methodological quality of the studies was evaluated using the PEDro scale and GRADE approach. The overall methodological quality of studies rated from moderate to high. Meta-analysis was not carried out due to the heterogeneity of included trials. The primary outcome measures of gait functions were the six-minute walk test, 10-meter walk test and Tinetti scale. Nine randomized controlled trials with 370 participants were analyzed. Out of them, eight studies proved its effectiveness on gait function on individuals with diabetic peripheral neuropathy. The finding of this study suggested that multi-component exercise therapy consisted of strength, ROM exercise, balance, flexibility and stretching exercises, circuit exercise training, and gait training found to enhance gait function for individuals suffering with diabetic peripheral neuropathy compared to control groups.

Keywords: exercise therapy, diabetic pain, functional training, gait, peripheral neuropathy, systematic review

Introduction

Diabetic peripheral neuropathy (DPN) is one of the long-term complications of diabetes caused by peripheral sensory and motor nerve dysfunction due to the disease sequelae.[1,2] This is the most common chronic complication, which could lead to morbidity and mortality in individuals with diabetes and that contributed a large economic burden for diabetes care.[3,4] Globally the estimated prevalence of DPN was 15.3–72.3/100,000 person-years.[5] In developing countries the prevalence of peripheral polyneuropathy in individuals with diabetes was approximately 25–50%.[4,6]

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DPN is a progressive degeneration of the peripheral nerves, particularly in the lower limbs,[7] which affects the sensory, motor, and autonomic components of the peripheral nerves, resulting in loss of protective sensation, intrinsic foot muscle dysfunction and anhydrosis of the foot.[8] DPN induces changes to the sensory and motor control system that affects the quantity and quality of the sensory information that is involved in the generation and control of the gait.[9] This can lead to reduced mobility and increases fall risk, which is related to reduced range of motion, muscle strength and changes in gait mechanics (gait cycle, decreased walking cadence and gait speed).[10–14]

Nowadays, several rehabilitation approaches were used for the treatment of DPNs. These include pharmacological drugs, manual therapy, electrotherapy modalities, acupuncture, and exercise therapy.[15–19] However; exercise therapy had great attention on improvement of gait function for individuals suffering with DPN.[20–22] Therapeutic exercise protocol, including range of motion exercise, muscle strengthening, circuit exercise training, gait and balance training. A prior review done on different exercise therapy had showed enhancements in the gait ability of physically frail older adults.[23] Moreover, Allet et al,[24] studied the intervention effect consisted of physiotherapeutic training, including gait and balance exercises with function orientated strengthening program geared to concurrently improving the balance and gait of diabetic patients. In contradiction to this, Sartor et al,[25] reported that a combination of stretching, strengthening, and functional foot and ankle exercises (twice a week over 12 weeks) had no significant improvement on foot function in subjects with DPN. Nonetheless, the efficacy of exercise therapy on gait function of individuals suffering with DPNs remains questionable.

Thus, to the extent of the authors' knowledge, there is a paucity of evidence on the effectiveness of exercise therapy on the gait function in patients with DPN in a systematic way. Therefore, the purpose of this review was to systematically summarize the recent randomized controlled trials (RCTs) on the effectiveness of exercise therapy programs on gait function in patients with DPN.

Methods

Design

This systematic review was conducted and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[26]

Searching Strategy

An electronic database, search by title and abstract was conducted in between October 2010 and May 2020 on the following databases: (1) PubMed, (2) the Cumulative Index to Nursing and Allied Health Literature (CINAHL), (3) The Allied and Complimentary Medicine Database (AMED), (4) Physiotherapy Evidence Database (PEDro), (5) ScienceDirect, (6) Google Scholar and (7) Cochrane Library. Specific search strategies depended on the particular database being searched. For the keywords and database search strategy we used the following: "Diabetic neuropathy"/"peripheral neuropathy" AND "gait function"; "gait therapy"/"gait rehabilitation";/"muscles strengthening exercises"/"exercise therapy"/"range of motion exercises"/"balance training"/"gait training"/ "Circuit training"/"sensor-based interactive exercise training" AND "RCTs". Hand searches of the reference list of included articles were also performed.

Eligibility Criteria

RCTs conducted to determine the effectiveness of exercise therapy on gait function in patients with DPN were included in this review. Only full-text articles published in English were included. Observational studies, quasi-experimental studies and conference abstracts were excluded from this review. Adult diabetic mellitus (DM) patients with peripheral neuropathy were considered. RCTs comparing the effectiveness of exercise therapy with the conventional therapy and/usual medical care/no intervention were included. Exercise therapy is defined as all rehabilitative exercise programs given to the DPN patients, which included at least one and or combination of two or more exercises of the following: muscle strengthening training, circuit exercise training, range of motion exercise, balance training exercise, flexibility and stretching exercises, gait exercise training, and sensor-based interactive exercise training.

Study Selection

One reviewer (HM) conducted the electronic database searches and screened the title and abstracts. Full texts of potential eligible articles were retrieved and independently screened by two reviewers (HM and AA). Disagreements were resolved by consensus without the need for a third reviewer (MH), who was available. Initial disagreements were due to intervention criteria,[27] study population,[28] study design.[29,30]

Risk of Bias in Individual Studies

The methodological quality of each of the included studies was evaluated using the PEDro scale,[31,32] and graded by two independent reviewers (HM and AA). The disagreement between the two authors was settled by consensus. PEDro scale is the most commonly used tools for quantifying the methodological quality of RCTs in physiotherapy.[33,34] It consists of a checklist of 10 scored yes-or-no questions pertaining to the methodological quality of RCTs.[32] It includes eligibility criteria, random allocation, concealed allocation, outcome measurement, similarity at baseline, greater than 85% follow-up for at least one outcome measure, intention-to-treat analysis, between-group statistical comparison and blinding (subject, assessor, and therapist). The overall quality of the evidence and the strength of recommendations were also evaluated using the GRADE approach.[35] The GRADE approach specifies four quality levels (high, moderate, low, and very low). The overall evidence was downgraded depending on the presence of five factors: limitations (due to risk of bias); consistency of results; directness (eg, whether participants are similar to those about whom conclusions are drawn); precision (ie, sufficient data to produce narrow confidence intervals); and other (eg, publication bias). (Table 1)

Data Extraction

The data extraction sheet has been developed based on the data retrieval template of the Cochrane Consumer and Communication Review Group. Two reviewers (HM and AA) extracted the data independently and the third author (MH) checked the extracted data. Disagreements were resolved by discussion between the review authors. The data were extracted from each RCT by using the following items: authors name and year of publication, diabetic neuropathy definition (Questionnaire of the Michigan Neuropathy Screening Instrument score, ability to walk, type of DM and duration), number of participants in both experimental and control groups, types of interventions in both experimental and control groups, mean follow-up time, mean age of the participants, treatment outcomes (baseline, follow-up and end of treatment), primary outcome measures, study design, study results, and conclusions.

Results

Study Selection

A search strategy of an electronic database found a total of 5882 articles. After adjusting for the duplicates, 2099 have remained. After the title and abstract screening among 803 studies, 758 studies were excluded. After full text screening out of 45 articles, 9 RCTs were included in this review (Figure 1).

Characteristics of the Included Studies

The detailed summary of the included trials is presented in Table 2. All selected studies were RCTs published in English. These studies have been published in Switzerland,[21] Netherlands,[36] Brazil,[25] Japan,[22] Italy,[37] USA,[38,39] and Egypt[40,41] between 2010 and 2019.

Nine RCTs with a total of 370 participants were analyzed. The mean age of participants in the experimental groups ranged from 65.2 (12.8)[38] to 73 (10)[37] and from 59 (11)[22] to 65.5 (13)[36] in the control groups. The minimum duration of DM since diagnosed was 2.4[22] and the maximum 27.2 years.[39] The primary outcomes were the six-minute walk test, 10-meter walking test, and Tinetti scale walk. The sample size of the participants in the included studies ranged from 27–71 individuals, in both the experimental and control groups.[21,37] The duration of the intervention ranged from 30–60 minutes for each session,[20,21,25,40] 2–5 times per week,[21,25,37] 2 to 24 weeks for both experimental and control groups.[22,36]

Risk of Bias of Included Studies

The risk of bias and methodological quality of the included studies are described in the Table 1. Randomization, baseline similarity, intention to treat analysis, between group comparison and point measures were assessed in all of the included studies. However, not all studies have reported on concealment allocations, blinding of therapists and patients. Four of the included trials have blinded the assessor.[25,37,38,41] The PEDro score of the included studies ranged from six to eight, with a mean score of seven that suggested the overall quality of studies. Based on the quality of the evidence and the strength of the recommendations, GRADE approach and PEDro score, the overall quality of the trails were ranged from moderate to high. (Table 1)

Interventions

The studies compared the effectiveness of exercise therapy and comparison/control group: pharmacological treatment and/self-care instructions and/neither treatment, nor specific advices were reviewed.

Table 1 Methodological Quality of Included RCTs

PEDro Scale Items	Allet et al, 2010[21]	Refay et al, 2013[20]	Mueller et al, 2013[38]	Sartor et al, 2014[25]	Taveggia et al, 2014[37]	Melai et al, 2014[36]	Grewal et al, 2015[39]	Suzuki et al, 2019[22]	Saleh et al 2019[40]
Eligibility	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Random allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concealed allocation	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes
Baseline comparability	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blind participants	No	No	No	No	No	No	No	No	No
Blinded therapist	No	No	No	No	No	No	No	No	No
Blinded assessor	No	No	Yes	Yes	Yes	No	No	No	Yes
Adequate followup	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention to treat analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Between group comparison	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Point estimates	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total score of quality	6/10	7/10	8/10	8/10	7/10	7/10	7/10	6/10	7/10
Graded approach	Moderate	Moderate	High	High	Moderate	Moderate	Moderate	Moderate	Moderate

Outcome Measures

Among the included trials four studies[20,25,36,40] measured gait function by using gait velocity and four studies[20–22,40] used cadence. Two studies[37,38] used ROM, 10-meter walking test and Tinetti scale to measure physical function and walking endurance. Only one study measured the gait function by using time spent in sitting, standing and walking (Appendix). [39]

Effects of Exercise Therapy on the Gait Function

Data extracted from the papers are summarized and presented in Table 2. Overall, all nine studies with 370 participants of DPN had investigated the effect of exercise therapy compared to control groups (no interventions/ pharmacological treatment/usual self-care on gait function.[20–22,25,36-40] Out of the included studies, eight of them (n=315) had confirmed that exercise therapy is effective on gait function for individuals suffering with DPN compared to the control groups.[20–22,36–40] But one study (n=55) reported that a combination of stretching, strengthening, and functional range of motion exercises (twice a week over 12 weeks) had no significant improvement on foot function in subjects with DPN.[25]

A total of seven studies (n=311) assessed gait function using gait assessment parameters (velocity (m/s), stride

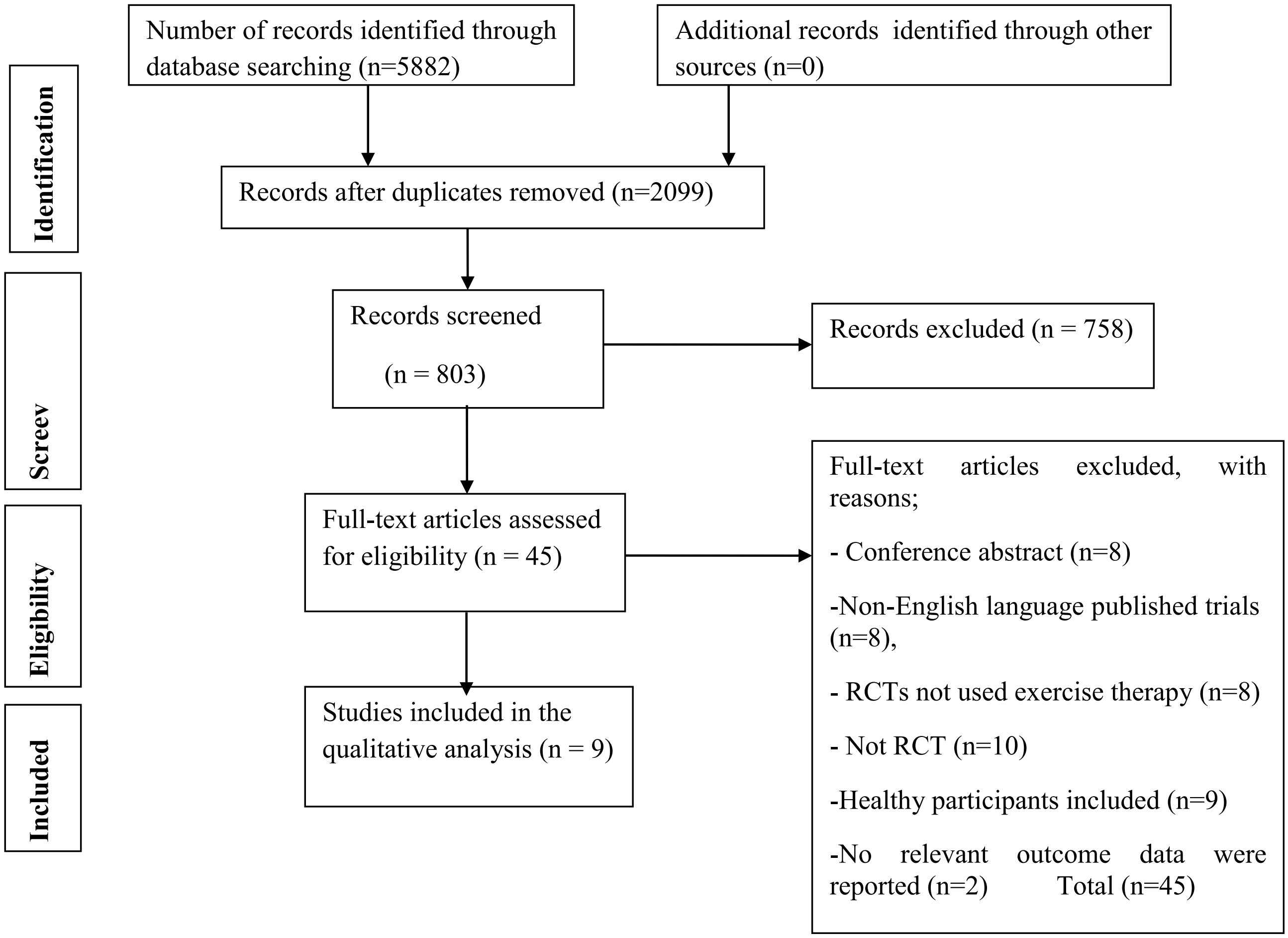

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) diagram.

length, step length, cadence (steps/min), step time (s), time-to-peak pressure (PP) and double support time (s),[20–22,25,36,39,40] and other two studies measured using the six-minute walk test, 10-meter walking test and theTinetti scale walk.[37,38]

Discussion

This systematic review evaluated the current evidence on the effectiveness of exercise therapy on gait function in patients with DPN. To the extent of the authors' knowledge, a systematic review of RCTs about exercise therapy in patients with DPN has not been performed yet. Therefore, the purpose of this review was to synthesize the effectiveness of exercise therapy on gait function in patients with DPN. The findings of this review demonstrated that exercise therapy had a beneficial effect in patients with DPN compared to the control groups. Out of nine studies, eight RCTs confirmed the effectiveness of exercise therapy on gait function in patients with diabetic neuropathy with a high methodological quality. The amount of exercise (dose) needed to achieve the desired improvements in gait function has not been determined and may vary from one patient to the next. In the reviewed studies, the time that participants engaged in exercise therapy ranged from 30 minutes to one hour at a time, twice to five times a week, and four weeks to 24 months duration. Due to the heterogeneity of the interventions, the gait functions of the participants were assessed using different outcome measures. All included studies investigated the posttreatment effect of exercise therapy on gait functions. For instance, the Refay et al,[20] study indicated that combinations of range of motion (ROM) exercises of lower extremity, muscle strengthening exercise for toes flexor/extensor and foot intrinsic muscle, balance training and gait training exercises improved walking speed, cadence and ankle range of motion with significant decrease of step time, while for the control group, no significant difference were noted. This might be due to

Table 2 Summary of the Included Studies in this Review

Author/ Years	Characteristics of the Participants	Outcome Measures	Interventions (Frequency, Type and Period of Follow-up)	Results	Conclusions
Allet et al, 2010[21]	Sample size: EG, n=35, CG, n=36 Mean age/years (SD): EG; n=63 (8), CG=64 (8.9) Sex (male %): not stated	Speed (ms^{-1}) Cadence (stride min^{-1}) Gait cycle time (s) Stride length (m)	EG= circuit training, including gait and balance exercises, twice a week for 60 min, over 12 weeks CG= received neither treatment, nor specific advice.	After intervention the IG increased their habitual walking speed by 0.149 ms^{1} (0.54 km/h^{-1}) on tarred terrain and by 0.17 ms^{-1} (0.61 km/h^{-1}) on the cobblestones. This significant treatment effect (P<0.004) decreased slightly in the six-month follow-up, but remained significant (P<0.004). In a similar manner significant improvement could be observed for cadence, GCT and stance time on both terrains. All, except stance time on the tarred terrain, remained significant at the six-month follow-up. Stride length showed a P-value <0.05, but failed to be significant at the corrected significance level of P<0.004. No significant effect was observed for coefficient of variation of gait cycle time on either surface	Gait, circuit, and balance training exercise combined with function-oriented strengthening can improve diabetic patients' gait
Refay et al, 2013[20]	Sample size: EG, n=15, CG, n=15 Mean age/years (SD): EG56.7 (0.3), CG=57.7 (4.2), =60; CG=46.	Velocity (m/s) Cadence (steps/min) Step time (s) Double support time (s) Ankle ROM (°)	EG=exercise intervention included: ROM exercises, muscles strengthening exercises, balance training and gait training three times a week, 45–60 min per session for eight weeks. CG=the usual recommended medical care, which included pharmacological treatment and self-care instructions, three times a week, 45–60 min per session for eight weeks.	In the EG, walking velocity, cadence was increased significantly (P=0.01, and 0.001 respectively) with percentage of change were 22.54% of velocity and 8% for cadence. step time was significantly decreased (P=0.03) with percentage of change was (–26.7%). In the CG, there was no significant change in any of the measured variables (P=0.2, 0.8, 0.1, and 0.8 respectively).	ROM, muscle strengthening, gait and balance exercises can improve gait of diabetic patients with peripheral neuropathy.

Mueller et al, 2013[38]	Sample size: EG, n=15, CG, n=14 Mean age/years (SD): EG=65.2 (12.8), CG=63.9 (12.5) Sex (male %): EG=66.6; CG=50	6MWD (m) Average daily step count (steps)	EG=received body-weight for resistance exercises (ie, sit to stand, stair climbing), and a treadmill or walking around a large circular hallway for aerobic exercise, one-hour per sessions three times/week for 12 weeks. CG=received all exercises in a sitting or lying position. They used elastic resistance bands with increasing stiffness for load resistance and a stationary upright or recumbent cycle ergometer for aerobic exercise.	The WB group showed greater gains than the NWB group over time on the 6MWD and average daily step count (*P*<0.05). The mean and 95%CIs between-group difference over time was 29 m (95%CI, 6–51) for the 6MWD and 1178 (95%CI, 150–2205) steps for the average daily step count. The NWB group showed greater improvements than the WB group over time in hemoglobin A1c values (*P*<0.05).	The results of this study indicate to increase 6MWD and daily step count with a WB exercise program compared with an NWB exercise program.
Melai et al, 2014 [36]	Sample size: EG, n=23, CG, n=30 Mean age/years (SD): EG=68.2 (12.9); CG=65.5 (13) Sex (male %): EG=83, CG=78	Gait velocity (m/s) Stride length Stride time	EG= received a warm-up with simple exercises during gait, followed by lower extremity muscle strength training three sets of 10 repetitions were performed for 24 weeks. CG=received no intervention	Experimental groups had a significant increase in stance phase duration, stride time and stride length of approximately 5%, during the imposed gait velocity. In both groups increased their preferred gait velocity over one year was observed.	Strength exercise showed changes in gait velocities and the progressive lower extremity problems in patients with polyneuropathy.
Taveggia et al, 2014[37]	Sample size: EG, n=13, CG; n=14 Mean age/years (SD): EG=73 (10) CG=71 (7) Sex (male %): EG=38.5, CG=35.7	Six-minute walk test, 10-meter walking test, Tinetti scale walk	EG=received a multimodal treatment consisting of 20 min of analyzing treadmill with feedback focused on symmetry and length of stride, 20 min of isokinetic dynamometric muscle strengthening 20 min of balance retraining on the dynamic balance platform, five days per week, for four weeks. CG=received activities targeted to improve the endurance, manual exercises of lower limb muscle strengthening and stretching exercises, five days per week, for four weeks.	The experimental group showed a significant increase in gait endurance in a six-minute walk test, 65.6 m; *P*=0.001). Six-minute walk test increased after the intervention, and an even greater difference was found at follow-up (*P*=0.005) for the standard care group. The Functional Independence Measure in both groups increased (*P*=0.01) and continued until the follow-up in the standard care group (*P*=0.003).	The results suggest that the experimental rehabilitation program showed positive effects on the gait endurance after four weeks of treatment, whereas it did not produce significant improvements of the gait speed.

(*Continued*)

Table 2 (Continued).

Author/ Years	Characteristics of the Participants	Outcome Measures	Interventions (Frequency, Type and Period of Follow-up)	Results	Conclusions
Sartor et al, 2014[25]	Sample size: EG, n=26; CG,; n=29 Mean age/years (SD): EG=59 (4), CG=60 (12) Sex (male %): EG=58, CG=48	Time-to-peak pressure (PP) Velocity (m/s) Total pressure – time integral (PTI) Functional tests	EG=started with passive exercises, progressed to active ones, and finished with walking and functional skills, 40–60 min per session, twice a week, for 12 weeks. CG=receive customized medical care and foot care instructions, 40–60 min per session, twice a week, for 12 weeks	Stride velocity was not statistically different between groups and assessments (group effect: P=0.57; time effect: P=0.13; interaction effect: P=0.61). After 12 weeks, there were increases in PTI in all foot regions, significant in the medial forefoot and hallux. The heel and toe areas displayed a medium effect size, and also showed increased PTI values after 12 weeks. An overall increasing tendency in PP was found in all foot regions after 12 weeks, but the increase was statistically significant only over the hallux.	The combination of stretching, strengthening and functional foot and ankle exercises provided modest changes in foot rollover. Pressure redistribution occurred in foot areas that are known to exhibit reduced participation in patients with DPN.
Grewal et al, 2015[39]	Sample size: EG, n=16, CG; n=19 Mean age/years (SD): EG=62.6 (7.9), CG=64.9 (8.5) Sex (male %): EG=50, CG=42.1	Time spent sitting, time spent standing, time spent walking Total steps	EG=received sensor-based interactive exercise training 45 min per session twice a week for four weeks. -CG=did not participate in any form of exercise	Compared with the CG, the patients in the IG showed a significantly reduced CoM sway (58.31%; P=0.009), ankle sway (62.7%; P=0.008) and hip joint sway (72.4%; P=0.017) during the balance test with open eyes. The ankle sway was also significantly reduced in the IG group (58.8%; P=0.037) during measurements while the eyes were closed. The number of steps walked showed a substantial, but nonsignificant increase (+27.68%; P=0.064) in the IG following training.	People with DPN can significantly improve their postural balance with diabetes-specific, tailored, sensor-based exercise training. The results promote the use of wearable technology in exercise training.
Suzuki et al, 2019[22]	Sample size: EG,; n=20, CG,; n=20 Mean age/years (SD): EG=59 (6), CG=59 (11) Sex (male %): EG=50, CG=65	Gait speed (m/s) Step length (m) Cadence (step/min)	EG=received a set of exercises aimed to muscle strength, balance, and physical endurance, as well as specific gait training, two weeks, (40 min/day) CG=did the same amount of walking as the RAS group, albeit without the metronome two weeks, (40 min/day).	RAS was associated with significant improvement in all parameters. In the control group, there was no improvement in cadence, co-contraction, or gait stability (vertical). Compared with the control group, the RAS group showed improvement in co-contraction and gait stability.	RAS may be helpful for improving the lower limb muscle coordination and gait function of DPN patients.

Saleh et al, 2019[40]	Sample size: EG,; n=15, CG,; n=15 Mean age/years (SD): EG=57.6 (4.9), CG=59.1 (4.2) Sex (male %): EG=46.6, CG=40	Step length (cm) Step time (sec) Double support time (sec) Velocity (cm/sec) Cadence (step/min)	EG=received the following exercises, active range of motion exercises for ankle and subtalar joints, functional balance training, gait training, 30 min per session three times a week for eight8 weeks. CG=received traditional physical therapy exercises only 30 min per session three times a week for eight weeks.	There was no significant difference between both groups in the pretreatment mean values of all measured variables. Significant improvement was observed in the two groups between pre- and posttreatment measured outcomes. Furthermore, the study group recorded significantly better improvement in all measured variables compared with the control group with diabetic neuropathy	Ankle proprioceptive training could be an excellent supplement to traditional physical therapy exercises used for improving gait and reducing risk of falling in patients.

Abbreviations: EG, experimental groups; CG, control groups; IG, interventional groups; WB, weight bearing; NWB, non-weight-bearing; 6MWD, 6-minute walk distance; CoM, center of mass; GCT, gait cycle time; RAS, rhythmic auditory stimulations; PTI, pressure time integral; ROM, range of motion; DNP, diabetic peripheral neuropathy.

exercise training, be able to improve macro and microvascular factors in diabetes.[42,43] Therefore, vascular adaptations caused by exercise may facilitate blood flow to peripheral nerves, moreover, it could improve gait function. Similarly, the study by Allet et al,[21] showed that gait and balance exercises with function-oriented strengthening, improved diabetic patients' gait functions compared with a control group of no treatment. Cadence contributed 80%, whereas stride length only contributed 20% to the change of gait velocity. This result was also supported by a study by Saleh et al.[40] This may be due to the treatment or to diabetic patients' potential to regulate their cadence and stride length. Stride length also tended to increase after the intervention, but was not significant at the corrected significance level. Whereas the study by Melai et al,[36] stated that stride length increases by 5% approximately in the exercise therapy group. It is supported by Gholami et al,[44] which found 7% improvement in HbA1c content following 12-week exercise training. Hence, it may be attributed to improved glucose control as a result of exercise intervention which could benefit gait function of subjects with DPN.[45]

Despite this, the study done by Sartor et al,[25] on the effects combination of strengthening, stretching and functional training on foot function in patients with diabetic neuropathy in intervention group primary outcome peak pressure (PP) reported that there was no statistically significant change under the six foot areas. The intention-to-treat comparisons yielded softening of heel strike (delayed heel time-to-peak pressure (TPP), better eccentric control of forefoot contact (decrease in ankle extensor moment, increase in function of ankle dorsiflexion), earlier lateral forefoot contact with respect to medial forefoot (TPP anticipation), and increased participation of hallux (increased PP) and pressure–time integral (PTI), and toes (increase in PTI, medium effect size). A slower COP mean velocity, and an increase in overall foot and ankle function were also observed, which may result from changes in the pressure variables in the foot.

Taveggia et al,[37] indicated that a combination of treadmill gait training, muscle strengthening and balance retraining showed a substantially greater improvement in gait endurance after four weeks compared to standard care. However, there was no significant improvement in gait speed.

Mueller et al[38] indicated that the weight-bearing exercise showed greater gait function improvement compared to the non-weight-bearing exercise group over time (significant interactions) in the primary outcomes of the six-minute walk distance (6MWD) and average daily step count. The mean between-group difference over time was 29 m (95%CI, 6–51) for the 6MWD and 1178 steps (95% CI) for the average daily step count. However, non-weight-bearing exercises showed greater improvements than the weight-bearing group over time (significant interaction) in hemoglobin A1C values. Nevertheless Grewal et al[39] stated that the number of steps walked showed a substantial, but nonsignificant increase (27.68%) in the intervention group following weight-bearing exercise training.

A study done by Suzuki et al,[22] showed that gait training exercises supported by rhythmic auditory stimulation over the two weeks of treatment improved gait parameters (ie, gait speed, step length, cadence) of DPN patients.

Taken together, most of the included studies highlighted that exercise therapy had significant improvement on gait function among subjects with DPN compared to the control groups.

Limitations of the Study

This review had the following limitations: this review included only English language published articles. Hence, there might be a chance of missing articles published in non-English languages. Due to the heterogeneity across the included studies, meta-analysis was not carried out.

Clinical Implication

This review indicates that, exercise therapy improved in gait parameters and physical function of patients with DPN. This systematic review suggests including exercise therapy in the rehabilitation programs, since it is feasible and beneficial for patients with DPN.

Conclusion

Exercise therapy is found to improve gait function of patients with DPN. Specific exercise training programs, including range of motion, muscle strengthening, circuit training, stretching exercise, gait, and balance exercises can improve gait of diabetic patients with peripheral neuropathy. Clinical decision-making should take into account the type and intensity of exercise and patient's tolerability related to each exercise.

Ethical Approval

Ethical approval or patient consent was not required, since the present study was a review of previously published literature.

Author Contributions

All authors' have contributed to the work reported, in the conception, study design, execution, acquisition of data, analysis and interpretation, drafted or written, or substantially revised or critically reviewed the article, agreed on the journal to which the article was submitted, reviewed and agreed on all versions of the article before submission, during revision. Finally, in any significant changes introduced at the proofing stage, the authors agree to take responsibility and be accountable for the contents of the article.

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Disclosure

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