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ORIGINAL ARTICLE

Randomized Controlled Trial

Effect of three-week exercise program on muscle strength and joint mobility in patients with diabetic polyneuropathy: Randomized controlled trial

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Abstract

BACKGROUND

Limited joint mobility is the proven risk factor for diabetic foot ulceration when present in the subtalar and first metatarsophalangeal joints. Evidence shows that a foot-related exercise program, combined with a health-promoting program, can improve the signs and symptoms of diabetic polyneuropathy, enhance gait, restore mobility in the foot and ankle joints, redistribute pressure while walking, and increase foot strength and function. As a result, these exercise programs can help mitigate the risk factors for diabetic foot ulceration.

AIM

To determine the effect of supervised stretching, strengthening, functional and walking exercises on joint mobility and muscle strength in patients with diabetic polyneuropathy.

METHODS

This was a randomized controlled trial conducted in a tertiary hospital. The study included 82 participants allocated into the intervention group (alpha-lipoic acid and exercise on 15 consecutive therapeutic days, n = 42) and control group (alpha

lipoic acid only, n = 40). Muscle strength included dorsal and plantar flexors dynamometry and strength score, while range of motion included ankle, subtalar and first metatarsophalangeal joint goniometry.

RESULTS

Change of motion range was significantly higher in the intervention group compared to the control group regarding ankle joint on day 15 (9.9 ± 7.2 *vs* 0.1 ± 3.3; P = 0.006) and month 6 (2.8 ± 7.3 *vs* -0.9 ± 4.1; P < 0.001), subtalar joint on day 15 (7.5 ± 5.1 *vs* -0.25 ± 2.25; P < 0.001) and month 6 (3.9 ± 6.4 *vs* -0.13 ± 3.49; P < 0.001). Change in dorsal flexors was significantly higher in the intervention group compared to the control group on day 15 (2.62 ± 1.69 *vs* 0.10 ± 1.35; P < 0.001) and month 6 (0.66 ± 2.38 *vs* -0.75 ± 1.94; P = 0.004) as well as plantar flexors on day 15 (3.3 ± 1.6 *vs* 0.3 ± 1.5; P < 0.001) and month 6 (1.8 ± 2.2 *vs* -0.9 ± 2.1; P < 0.001). Muscle strength score change was significantly lower in the intervention group compared to the control group on day 15 (-1.45 ± 1.42 *vs* -0.03 ± 0.16; P < 0.001) and month 6 (-1.17 ± 1.53 *vs* 0.20 ± 0.56; P < 0.001).

CONCLUSION

Exercise in combination with alpha-lipoic acid can improve joint mobility, as well as strength of the foot and lower leg muscles in patients with diabetic polyneuropathy.

Key Words: Diabetes; Diabetic polyneuropathy; Diabetic foot ulcer; Muscle strength; Range of motion; Exercise

Core Tip: Improvement in biomechanical parameters, while enhancing mobility and overall patient condition, has the potential to reduce the risk of developing diabetic ulcers in patients with diabetic neuropathy. A combined and supervised exercise program lasting 15 therapy days, consisting of stretching, strength, functional and walking exercises, can improve the mobility in the ankle, subtalar and first metatarsophalangeal joint, as well as the strength of the foot and lower leg muscles in patients with diabetic peripheral neuropathy. The effects achieved by this treatment can last up to 6 months after the intervention.

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INTRODUCTION

More than one in ten adults worldwide are currently living with diabetes, resulting in direct health expenditures approaching one trillion United States dollar[1]. Among all individuals with diabetes, the lifetime risk of developing a diabetic foot ulcer is 25%[2], with an alarming statistic suggesting that every 30 seconds a lower limb is amputated somewhere in the world due to diabetes[3]. It is worth noting that diabetic foot ulcer (DFU) prevention receives minimal attention, both in clinical practice and scientific research, indicating an urgent need for a shift in priorities[4].

Diabetic peripheral neuropathy (DPN) is subdivided into sensory, motor, and autonomic neuropathy, which can lead to a loss of protective sensation, biomechanical abnormalities, and skin changes[2]. These neuropathy-related changes affect the form and function of the foot, including reduced range of motion (ROM), development and progression of foot deformities, decreased strength and function of the distal muscles, and alterations in foot rollover during gait[5-8]. Such abnormalities disrupt the normal mechanical loading on the foot, increasing the risk of ulceration[6,9-11]. Biomechanical alterations stemming from DPN may elevate plantar pressures in the foot, thereby contributing to the pathogenesis and development of DFU[6].

There are significant associations between polyneuropathy, reduced muscle strength (MS) and atrophy in the legs[12]. This atrophy is most notable in the distal muscles of the lower leg, indicating a neuropathic process that is dependent on length[13]. The atrophy of small muscles in the foot leads to a decrease in supportive surface area[13], causing deformation of the metatarsal heads and subsequently excessive plantar loads during gait, which predisposes individuals to callus formation, hyperkeratosis, and ulcers[14]. Reduced MS around the ankle joint (AJ), particularly in the tibialis anterior, may account for gait abnormalities observed in diabetic patients[5], particularly during the early stance phase when the ankle and tibialis anterior play crucial roles in controlling foot flattening[15].

Limited joint mobility is identified as a confirmed risk factor for ulceration only when it affects the subtalar and first metatarsophalangeal joints (I MTP)[7]. When joint mobility is reduced, the foot may lose its capacity for proper shock absorption and fail to maintain normal plantar pressure, potentially increasing the risk of trauma to the plantar surface and the development of ulceration. Within this framework, exercise has consistently been recognized as a crucial element in both prevention and therapy[12].

There is significant evidence supporting the effectiveness of foot-related exercise programs when combined with health-promoting interventions in improving neuropathy signs and symptoms, enhancing gait, restoring foot and AJ mobility, redistributing pressure during walking, and increasing foot strength and function. These combined efforts can help mitigate risk factors for DFU[16-19]. Considering that DPN is a chronic condition, with complications in muscles and joints developing over the long term, preserving and maintaining their integrity is of paramount importance[5,20].

It is expected that specific interventions could lead to the recovery of muscle and joint function in patients with DPN [20]. The objective of this study was to determine the effect of supervised stretching, strengthening, functional, and walking exercises on joint mobility and MS in patients with DPN.

MATERIALS AND METHODS

This two arm, parallel design, randomized clinical trial was conducted from February 2020 to October 2022 at the Outpatients Clinic of the Institute for Physical Medicine, Rehabilitation and Orthopedic Surgery "Dr Miroslav Zotović" Banja Luka, the Republika Srpska, Bosnia and Herzegovina (referred to in the following text as Institute). The Institute where the study was conducted was chosen as it employs the researchers and most of the authors, and because it provides kinesitherapy and alpha-lipoic acid (ALA) therapy. The clinical trial was approved by the ethics committees of the institute, protocol number: No. 116-31-3090-1/20, and Faculty of Medicine, University of Banja Luka, protocol number: No. 18/4.3.13/20. The trial is registered in ANZCRT with registration number ACTRN12624000844549.

Patients who were referred to the institute for treatment of DPN with ALA and physical therapy were invited to participate in the study. All eligible patients, who were willing to participate, and who fulfilled the inclusion criteria and signed the informed consent, regardless of nationality or religion were enrolled in the study. Inclusion criteria were as follows: Age between 40 and 65 years, diabetes mellitus (DM) type 1 or 2 diagnosed for at least five years, stable glycemic control, body mass index ranging between 18.5 and 29.9 kg/m^2 (normal and overweight), electroneurographic findings indicating the presence of DPN and the ability to walk independently, without any device. Patients were excluded from the study if they had any of the following: Unstable glycemic control, active ulcers, amputations, central neurological impairments, peripheral neurological impairments other than DPN, orthopedic diseases or previous surgeries, rheumatological diseases affecting movement, severe vestibular or ocular impairments affecting movement, severe nephropathy or DPN, unresolved pain of unknown etiology, intermittent claudication, an ankle-brachial index less than 0.8 or greater than 1.2, malignancy, or pregnancy. All participants in the study were fully informed about every aspect of the research process and provided their signed informed consent.

The study was not supported by financial means from any source, and the participants did not receive any financial compensation.

Of the total 102 screened patients, 90 patients were included in the study. The participants were randomly allocated into the intervention group (IG) or the control group (CG) using sealed envelopes with 45 patients in each group. In total, four patients were discontinued and four were lost in follow-up. The final analysis sample consisted of 42 participants in the IG and 40 in the CG. The design of the study, the dropouts and refusals are presented in Figure 1.

The participants in both groups continued their prescribed pharmacological treatment and self-care instructions without changes.

Patients in the IG received ALA intravenously at a dose of 600 mg dissolved in 250 mL of 0.9% sodium chloride solution, administered over 60 minutes. Additionally, they participated in a 50-60 minutes daily exercise program for 15 consecutive therapy days, excluding weekends, during intravenous ALA therapy.

The intervention comprised a specific kinesiotherapy program consisting of four exercise blocks, each targeting different objectives: (1) Increasing foot and ankle ROM; (2) Strengthening foot and ankle muscles; (3) Performing functional exercises for the foot and ankle; and (4) Training walking skills and foot rollover[20]. This intervention began immediately after patients were assigned to the IG.

Each session was composed of some of the exercises from the four groups. Gradual and progressive difficulty was offered to the patient, respecting any limitation due to pain and/or decrease in performance during execution. The ROM exercises included passive exercises for the hallux and toe joints, as well as active exercises for the AJ and subtalar joint (SJ), lasting about 20 minutes. Strengthening exercises for the hallux and toe flexors, as well as the intrinsic foot muscles, were performed actively using objects of varying rigidity. Exercises for the hallux and toe extensors were done actively without resistance. To strengthen the flexors, extensors, invertors, and evertors of the ankle complex, theraband bands of varying resistance levels and the patient's body weight were used, with an appropriate number of repetitions for each movement, lasting approximately 15 minutes. Functional foot exercises and balance training involved maintaining balance on one leg with and without support from the upper extremities, and balancing on a rubber disc for a set number of repetitions, totaling about 7 minutes. Walking exercises included walking on the heels, forefoot, lateral and medial borders of the foot, tandem walking, softening the heel and forefoot contact during normal walking, grabbing the floor with the toes, and walking with a considered normal foot rollover (heel strike, midfoot, lateral forefoot, medial forefoot, and hallux contact), lasting a total of approximately 15 minutes. In addition, in each session, the exercises were performed following an order that started with the passive exercises, progressed to active, and finished with walking and functional skills[20,21]. The complete intervention protocol has been published elsewhere[21] and the exercises were individually adjusted to each patient, guided and supervised by a physiotherapist. The physiotherapist monitored the patient's general condition, paying close attention to any signs of pain and fatigue, passive exercises were performed to increase the ROM, carefully managing the number of repetitions and duration of each exercise, and progress in MS was tracked to gradually introduce greater resistance. After the 15 days program, patients were advised to continue with the learned

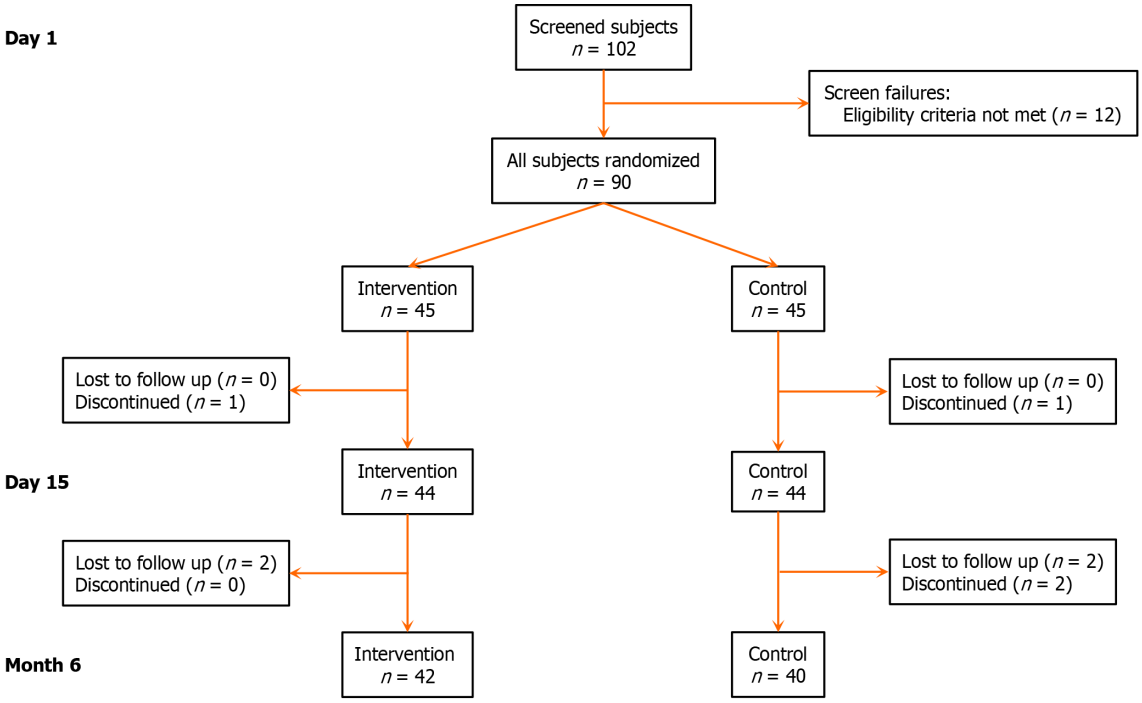

Figure 1 The study flow chart.

exercises during the next 6 months and no other advice or restrictions were provided.

The patients in the CG received ALA at the same dose and administration as in the IG but did not undergo any physical therapy intervention[22-25].

The clinical report form comprised a review of medical records, gathering anamnestic data including medical history, as well as the measurement and testing of patients. Baseline examination medical records provided personal data, with details regarding the type of DM, duration and management of the disease to date, and glycated hemoglobin (HbA1c) values not exceeding six months old[26,27].

ROM and MS assessments were conducted by the same examiner at three time points: Baseline (D1), after 15 therapy sessions (D15), and six months post-completion of therapy (M6) for post-intervention evaluation.

ROM measurement

ROM measurements were conducted for the AJ, SJ and I MTP using a goniometer on the dominant lower limb[28,29]. For the AJ, ROM was assessed with the patient in the supine position. The passive maximum range of talar flexion and extension were measured, and their sum was recorded as the ROM at the AJ[28]. The ROM at the SJ was evaluated with the patient in the prone position. The maximum range of calcaneal inversion and eversion were measured, and their sum indicated the ROM at the SJ. Lastly, the range of passive extension to plantar flexion at the I MTP was measured with the patient supine, and the ROM at the I MTP was recorded as the sum of those two values[28,29].

MS assessment

MS assessment of the foot and ankle was conducted using a hand-held dynamometer and manual muscle testing (MMT) on the dominant leg. MS of the plantar flexors (MSPF) and MS of the dorsal flexors (MSDF) represented the maximum isometric strength of the dorsal flexor muscle group and plantar flexor muscle group, respectively. These measurements were performed with a hand-held dynamometer (Baseline push-pull 1001b, United States) and expressed in kilograms [30]. The measurements were taken with the patient in the supine position and the foot in a neutral position. The dynamometer's board was placed perpendicular to the plantar and dorsal surfaces of the foot, respectively. Patients were instructed to exert maximum isometric contraction while the examiner applied resistance to prevent foot movement. A one-minute rest period was given between consecutive trials. Patients performed three efforts for each muscle, and the best reading among the three trials was recorded[31].

The scoring system utilized in the Michigan diabetic neuropathy score was applied[21,32,33] to derive the score of MS (SMS). MMT was used to assess the muscle's ability to generate active movement against the examiner's resistance. The scoring system was as follows: Score 0 indicated normal MS, 1 signified mild weakness, 2 indicated severe weakness, and 3 represented complete loss of MS. The SMS was determined for each set of muscles examined. The minimum score was 0, indicating normal strength in 10 muscles, while the maximum score was 30, indicating complete loss of strength in 10 muscles. Higher scores indicated greater muscle weakness[32]. MMT was performed for the following muscles in the described positions: Triceps surae, tibialis anterior, interosseus, lumbrical, flexor hallucis brevis, extensor digitorum brevis, extensor digitorum longus, flexor digitorum brevis, extensors hallucis longus, and extensor hallucis brevis[21].

Statistical analysis

Statistical analysis was performed by a biomedical statistician. The sample size was calculated using formula for two independent samples *t* test. Assuming -2 and 0 (common SD = 3) in MS change on day 15 in the IG and CG, type I error alpha = 0.05, type II error beta = 0.2 and allocation ratio 1, 37 participants was sufficient to achieve 80% study power. Assuming possible dropouts, 45 participants were planned for recruitment, to preserve study power in the case of 20% drop-outs.

Results are presented as count (%), means ± SD or median (interquartile range) depending on data type and distribution. Groups were compared using parametric (*t* test) and nonparametric (χ^2 test, Mann-Whitney *U* test) tests. All *P* values less than 0.05 were considered significant. All data were analyzed using statistical product and service solutions (SPSS) 29.0 (International Business Machines Corporation Released 2023. International Business Machines Corporation SPSS Statistics for Windows, Version 20.0. Armonk, NY, United States) and R 3.4.2. (R Core Team 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

RESULTS

The baseline characteristics of the participants showed that both groups had similar gender and age distributions, as well as distributions and durations of diabetes types 1 and 2, glycemic control (HbA1c), and types of hypoglycemic treatment. The only notable difference was a slightly higher frequency of ulcers in the IG, although this difference was not statistically significant (Table 1).

The average values of AJ, SJ, and I MTP at baseline were similar in both groups, with slightly higher average values in the CG, although this difference was not significant. On day 15, significantly higher average levels of the AJ and SJ were observed in the IG. After six months, AJ and I MTP average values were higher in the IG, but without significance, while SJ remained statistically significant. When changes in values were analyzed, significant differences between the groups were observed in the D15-D0 change in AJ, SJ, and I MTP, while M6-D0 significant differences were observed in AJ and SJ (Table 2).

Average baseline levels of MSDF, MSPF and SMS were significantly higher in the CG, compared to the IG. On D15, the values of both MSDF and MSPF were converging, but again, were significantly lower in M6 in the IG. When the change in values was evaluated, the significantly higher average values were observed in the IG, both in D15-D1 and M6-D1 (Table 3).

The average baseline levels of MSDF, MSPF and SMS were significantly higher in the CG compared to the IG. On day 15, the values of both MSDF and MSPF were converging, but again, they were significantly lower in the IG at six months. When the change in values was evaluated, significantly higher average values were observed in the IG, both in the D15-D1 and M6-D1 intervals (Table 3).

DISCUSSION

Understanding and studying the mechanisms of ulcer development, including the biomechanical components is crucial[6,14], as early prevention, involving diabetes control and inducing biomechanical changes, can reduce the risk of DFU and their recurrence[34]. The present study evaluated the effects of supervised structured therapeutic exercises, consisting of ROM, muscle strengthening, functional, and gait exercises, on joint mobility and MS in patients with DPN. The outcome measurements included ROM at the AJ, SJ, and I MTP, as well as foot and ankle MS. The results of the present study revealed that joint mobility and MS of the lower leg and foot muscles in patients with DPN can be improved by an exercise rehabilitation program. In the IG, ROM at AJ, SJ, and I MTP, as well as MS, significantly increased after the intervention compared with baseline. Despite a reverse tendency observed after 6 months, the intervention effect remained significantly different in the ROM at AJ and SJ, as well as MS, during the post-intervention evaluation.

The examined groups showed similar baseline characteristics. Randomization was expected to achieve homogeneity among patients regarding age, gender, duration of DM, HbA1c levels, and therapy, resulting in comparable study arms. Many studies with similar aims utilize randomized intervention-control, parallel-design clinical trials[12,20,34-36]. With similar baseline characteristics, the true effect of the intervention is observed without being obscured by other confounding factors. During exercise, no adverse events were reported. However, three participants in the CG were lost due to leg injuries sustained outside the exercise room, one during treatment and two between the intervention and the 6-month follow-up examination. All outcome measurements were conducted by a single individual, suggesting that error margins in assessment could be expected to be similar in both groups.

Several studies have examined treatments aimed at enhancing joint mobility and MS in patients with DPN. However, there is considerable variation in the duration and composition of training among these studies, making direct comparisons difficult.

Dijs *et al*[35] investigated the intervention effect of a physical therapy program involving passive joint mobilization administered at a rate of two sessions *per* week. They demonstrated significant improvement in joint mobility at the AJ, SJ, and I MTP after 10 sessions. They found that the increased mobility of these joints was sustained three months post-therapy, with significant differences in ROM at the SJ and I MPT observed six months after therapy completion. Sartor *et al*[21] and El-Refay and Ali[5] studied the effect of a specific exercise program comprising ROM, muscle strengthening, walking, and balance exercises on ROM at the AJ. Sartor's study involved subjects with DPN exercising twice a week for

Table 1 Baseline characteristics of the patients, *n* (%)

	Intervention (*n* = 42)	Control (*n* = 40)	*P* value
Gender male	31 (73.8)	33 (82.5)	0.342[1]
Age, mean ± SD (years)	56.62 ± 7.76	56.68 ± 8.27	0.975[2]
DM			
Type 1	5 (11.9)	8 (20)	0.316[1]
Type 2	37 (88.1)	32 (80)	
HbA1c, mean ± SD (%)	7.93 ± 1.89	7.49 ± 1.71	0.414[2]
DM duration (years)	14 (10)	12 (15)	0.705[3]
Oral hypoglycemics (years)	10.5 (8)	10 (9)	0.971[3]
Subcutaneous hypoglycemics (years)	6 (10)	8.5 (20.5)	0.098[3]
Insulin pump	1 (2.4)	2 (5)	0.611[4]
Ulcer	6 (14.3)	1 (2.5)	0.110[4]

[1]*P* calculated by χ^2 test.
[2]*P* calculated by *t* test.
[3]*P* calculated by Mann-Whitney *U* test.
[4]*P* calculated by Fisher's Exact test.
DM: Diabetes mellitus.

12 weeks[21], while in the study by El-Refay and Ali[5], subjects exercised three times a week for 8 weeks[5]. Both studies reported a significant increase in ROM at the AJ. Additionally, Francia *et al*[12] and Monteiro *et al*[37] also found significant improvement in AJ mobility after a 12-week training program. However, Monteiro *et al*[37] found no differences between groups in terms of ROM at the AJ during the 24-week and 1-year follow-ups. Cerrahoglu *et al*[8] determined an increase in ROM at the AJ and I MTP after a four-week foot-targeted home exercise program, comprising ROM, stretching, and strengthening exercises in diabetic patient groups, irrespective of the presence of DPN[8]. Similarly, Goldsmith *et al*[38] reported increased ROM at the AJ following four weeks of unsupervised range-of-motion exercise in diabetic subjects. Kanchanasamut and Pensri[36] investigated the effects of an 8-week weight-bearing exercise program on a mini-trampoline and found a significant improvement in ROM at the I MTP. However, only one study reported no differences in ankle or foot mobility after an unsupervised lower limb home exercise program lasting 10 months[39].

All the above-mentioned studies confirmed the positive effect of exercises on increasing the mobility of one or all joints examined in the present study. However, there are differences in the duration and supervision of the therapeutic interventions compared to our study. In the study by Dijs, duration of the intervention was shorter, while in other studies, duration of the interventions was longer[35]. Comparing these results is difficult as some authors conducted supervised exercise programs, while others conducted partially supervised exercise programs. It is important to note that in the study examining the effects of a supervised exercise program consisting of 20 consecutive sessions, there was maintenance of joint mobility 6 months after the intervention[35], as demonstrated in this study for the AJ and SJ joints. However, the study examining the effects of a 12-week exercise program, performed twice weekly under in-person supervision by a physiotherapist, and twice weekly at home, remotely supervised through the corresponding software [39], did not demonstrate maintenance of effect 6 months after the intervention.

The results of the study conducted by Francia *et al*[12] showed that a 12-week exercise therapy intervention, tailored to the subject's condition, can improve MS of ankle flexors[12]. Similarly, Allet *et al*[30] demonstrated that physiotherapeutic group training, including gait and balance exercises with function-oriented strengthening, conducted twice weekly over 12 weeks, can improve hip and ankle strength as well as ankle mobility. However, the strength and mobility effects did not remain significant at the 6-month follow-up[30]. Vrátná *et al*[34] observed significant improvement in MS in participants included in an age-appropriate structured intervention exercise program, which lasted for 12 weeks and was conducted four times a week[34]. However, Kruse *et al*[40] studied the effect of a physical therapy program consisting of eight individual sessions with a physical therapist focused on exercises to progressively strengthen legs and improve balance, with an additional three weekly sessions of 1 hour each at home but did not demonstrate improvement in lower extremity MS and balance.

All the above-mentioned studies demonstrated the effect of different exercise programs on increasing MS, as shown in the present study, except the study conducted by Kruse *et al*[40]. Therefore, to improve strength, balance, and gait in patients with DPN, he recommended a supervised, center-based exercise program instead of a self-administered, home-based program[40]. However, the therapeutic intervention in all mentioned studies lasted longer, and none of them examined the maintenance of effect 6 months after the intervention.

The majority of DFUs develop as a result of the repetitive action of mechanical stress (pressure) during gait in the presence of DPN or loss of protective sensation[6,41]. Lower extremity muscle problems are important risk factors for DFU development that directly influence altered foot biomechanics and abnormal foot loading[42,43]. Muscle atrophy

Table 2 Range of motion examination, mean ± SD

	Intervention (*n* = 42)	Control (*n* = 40)	*P* value
Ankle joint			
D1	46.64 ± 11.7	47.9 ± 10.03	0.604
D15	56.55 ± 11.66	48 ± 9.99	< 0.001
M6	49.4 ± 12.7	47 ± 9.25	0.332
D15-D1	9.9 ± 7.16	0.1 ± 3.26	< 0.001
M6-D1	2.76 ± 7.26	-0.9 ± 4.06	0.006
Subtalar joint			
D1	21.43 ± 6.22	23.13 ± 6.47	0.230
D15	28.93 ± 4.49	22.88 ± 6.29	< 0.001
M6	25.4 ± 4.28	23 ± 5.97	0.039
D15-D1	7.5 ± 5.12	-0.25 ± 2.25	< 0.001
M6-D1	3.98 ± 6.4	-0.13 ± 3.49	< 0.001
First metatarsophalangeal joint			
D1	73.81 ± 17.03	78.65 ± 19.52	0.234
D15	83.88 ± 17.51	80.63 ± 15.49	0.376
M6	75.55 ± 16.77	77.5 ± 19.81	0.631
D15-D1	10.07 ± 18.66	1.98 ± 8.39	0.014
M6-D1	1.74 ± 19.72	-1.15 ± 13.81	0.447

P calculated by independent samples *t* test. D: Day; M: Month; D15-D1: Change in values at day 15 compared to baseline (day 1); M6-D1: Change in values at month 6 compared to baseline (day 1).

and muscle imbalance also play an important role in the genesis of foot deformities and it has been hypothesized that the loss of foot muscles precedes the development of toe abnormalities and metatarsal prominence, thus increasing the risk of ulcer[11]. Limited joint mobility is correlated to the foot's peak plantar pressure, pressure–time integrals and shear forces [28,29,44]. Due to the reduction of ROM at the AJ, the foot rollover is disturbed in a way that foot landing occurs with the most anterior part of the heel[45-47]. The ROM deficit at the SJ increases the difficulties in inversion/eversion affecting the foot-rolling during mid-stance, does not allow proper preparation of the push-off[44,47] and causes a greater plantar pressure and abnormal gait in diabetic patients[11]. Reduced ROM at I MTP induces altered foot propulsion and increases the load at the metatarsal heads[28,46], consequently, the load is accumulated at the forefoot during the whole stance phase[44,45].

There is still a gap in the literature regarding whether specific training aimed at improving ROM and MS could effectively reduce the risk of ulceration in the long-term. Only one study showed that foot and ankle exercises can reduce the recurrence of DFU[16]. The evidence we obtained in this study supports the thesis that it is possible to successfully treat musculoskeletal impairments in patients with DPN. This provides additional support for the paradigm shift toward exercise as a primary treatment approach for people with DPN[48] as exercise, among other positive effects, can mitigate the risk factors for DFU[9,18]. Considering that biomechanical factors, such as impaired ROM and reduced MS, contribute to the development of DFU by causing abnormal levels of plantar pressure and pressure distribution[9,11], and that there is potential for recovery of these factors through exercise, it can be reasonably assumed that the risk of foot ulceration will decrease with improvements in ROM and MS.

Continued research is necessary to gather ample evidence on the effectiveness of diverse rehabilitation programs for patients with DPN and preventing other diabetes-related complications, particularly ulcers and amputations. Improved ROM and MS are anticipated and demonstrated outcomes of training involving stretching and strength exercises. However, concerns are related to the format and duration of the intervention, as well as the sustainability of its effects. Standardizing exercise protocols would also facilitate accurate comparison of results.

The main limitation of this study is that the measurement was performed manually, *i.e.* using a goniometer and a hand-held dynamometer, but bearing in mind that one examiner made all measurements, potential error occurred in all subjects. This limitation certainly affects the precision and consistency of the collected data. In the future, we should aim to conduct studies using validated and calibrated devices to completely eliminate examiner bias and reduce the possibility of measurement errors. However, it is not necessary to entirely exclude measurements obtained with hand-held devices, such as dynamometers and goniometers, as these tools are widely available and practical in various settings where healthcare services are provided to patients with diabetes. No monitoring of home exercises can be considered a

Table 3 Foot and ankle muscle strength examination, mean ± SD

	Intervention (*n* = 42)	Control (*n* = 40)	*P* value
Dorsal flexors			
D1	13.12 ± 4.46	16.5 ± 4.18	< 0.001
D15	15.74 ± 4.7	16.6 ± 4.27	0.388
M6	13.79 ± 3.65	15.75 ± 3.87	0.021
D15-D1	2.62 ± 1.69	0.1 ± 1.35	< 0.001
M6-D1	0.66 ± 2.38	-0.75 ± 1.94	0.004
Plantar flexors			
D1	20.95 ± 6.16	26.61 ± 5.78	< 0.001
D15	24.19 ± 6.03	26.91 ± 5.88	0.042
M6	22.74 ± 5.56	25.63 ± 5.66	0.022
D15-D1	3.24 ± 1.62	0.3 ± 1.48	< 0.001
M6-D1	1.79 ± 2.18	-0.99 ± 2.08	< 0.001
Score of muscle strength			
D1	13.93 ± 4.41	10.33 ± 4.13	< 0.001
D15	12.48 ± 3.84	10.3 ± 4.15	0.016
M6	12.76 ± 3.82	10.53 ± 4.27	0.014
D15-D1	-1.45 ± 1.42	-0.03 ± 0.16	< 0.001
M6-D1	-1.17 ± 1.53	0.2 ± 0.56	< 0.001

P calculated by independent samples *t* test. D: Day; M: Month; D15-D1: Change in values at day 15 compared to baseline (day 1); M6-D1: Change in values at month 6 compared to baseline (day 1).

limitation of this study. This limitation makes it difficult to determine how many participants followed the recommendations, how often they exercised at home, the extent to which they performed the exercises, and how these factors impacted the measurement results six months after the therapy concluded. Nonetheless, even without monitoring home exercises, it is important to highlight that the effects of the 3-week exercise program persisted for six months, except for the change in the I MTP joint. This finding is significant given the high prevalence of diabetes and the limited availability of rehabilitation resources. Bearing in mind that the inclusion and exclusion criteria for this study were quite strict when it comes to age, body weight, glucose regulation, *etc*, the question arises whether the results would be equally good in patients with DPN who have a worse general condition, DFU or amputation.

The exercise program's effectiveness in this study likely stems from its incorporation of not only stretching and strength exercises but also functional and gait exercises. Moreover, the program duration spanned 15 consecutive days, excluding weekends, with exercises individually tailored, guided, and supervised by a physiotherapist. While the relatively short duration of the program presents an advantage compared to other studies with similar effects, such a regimen necessitates implementation within rehabilitation or specialized centers. With the consideration of sustaining effects even 6-months post-intervention, apart from the ROM at I MTP joint, the therapeutic approach in this study appears favorable and thus acceptable. Due to its relatively short duration and ease of learning and performing at home, this relatively simple exercise protocol can be applied during various other therapeutic procedures.

CONCLUSION

A combined and supervised exercise program lasting 15 therapy days, consisting of stretching, strength, functional and walking exercises, can improve the mobility in the ankle, subtalar and I metatarsophalangeal joint, as well as the strength of the foot and lower leg muscles in patients with DPN. The effects achieved by this treatment can last up to 6 months after the intervention. Every improvement in biomechanical parameters, while enhancing mobility and overall patient condition, has the potential to reduce the risk of developing diabetic ulcers, which is a major task for medical science and the medical profession. In pursuit of that goal, it is necessary and beneficial to introduce exercises in patients alongside other therapies, as a multifaceted and efficient therapeutic modality.

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FOOTNOTES

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