Multimodal Treatment of Distal Sensorimotor Polyneuropathy in Diabetic Patients: A Randomized Clinical Trial

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Abstract

Objective: The purpose of this study was to evaluate the effectiveness of the application of analyzing treadmill, muscle strengthening, and balance training compared with a standard care intervention in patients with diabetic neuropathy.

Methods: Twenty-seven patients, 63% female (mean ± standard deviations age, 72 ±9 years), with diabetic neuropathy randomly assigned to receive a multimodal manual treatment approach including analyzing treadmill with feedback focused, isokinetic dynamometric muscle strengthening, and balance retraining on dynamic balance platform or a standard care intervention for activities targeted to improve endurance, manual exercises of muscle strengthening, stretching exercises, gait, and balance exercises (5 weekly over 4 weeks). This study was designed as a double-blind, randomized clinical trial. Measures were assessed at pretreatment, 4 weeks posttreatment, and 2-month follow-up.

Results: No important baseline differences were observed between groups. At the end of the treatment period, the experimental group showed a significant increase in gait endurance in a 6-minute walk test, 65.6 m ($F_{[2.0]} = 9.636$; $P = .001$). In addition, the 6-minute walk test increased after the intervention, and an even greater difference was found at follow-up ($P = .005$) for the standard care group. The Functional Independence Measure in both groups increased ($P < .01$) and continued until the follow-up in the standard care group ($P = .003$).

Conclusions: The results suggest that the experimental rehabilitation program showed positive effects on the gait endurance after 4 weeks of treatment, whereas it did not produce significant improvements of the gait speed. Both the treatments produced significant improvement of functionalities of the patient. (J Manipulative Physiol Ther 2014;37:242-252)

Key Indexing Terms: *Gait Disorders; Neuropathy; Muscle Strength; Walking*

Diabetic neuropathy is a neuropathic disorder associated to diabetes mellitus, and it involves damage to nerve fibers or entire nerve cells.[1] Distal sensorimotor polyneuropathy (DSP) is the most common cause of neuropathy and affects 50% of diabetic patients over the age of 60 years.[2] This type of neuropathy produces peripheral damage (distal neuropathy), and it is a result of a systemic process (polyneuropathy) affecting the nerves related to touch (sensory neuropathy) and that cause movement (motor neuropathy).[1] Muscle weakness is found in diabetic patients with DSP, whereas non-neuropathic patients even with long-term diabetes show a muscle strength compatible with their age. The weakness is therefore correlated to the severity of DSP.[3]

Diabetic patients respond to resistance and aerobic training, which improve their metabolic and functional conditions and, in particular, opposing to the devastating decrease in muscle performance in DSP.[4] Focusing on motor disability, rehabilitation science has explored various treatments, with the aim of preserving gait functions and preventing falling risks. Recent literature on the topic recommends balance retraining exercises, muscle strengthening, selective stretching, and retraining of motor activity.[5] One field of research in rehabilitation science stresses the possibility of the use of technology,[6] and several studies are

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devoted to comparing technological treatments with other control treatments. Distal sensorimotor polyneuropathy can benefit from electromechanical dynamometers (for strengthening exercises), balance platforms (for balance recovery), and analyzing treadmills (for gait training). These technologies are often used in the rehabilitation of patients but are rarely used in DSP.

Elderly adults with diabetes walk slower, take shorter strides during all walking conditions, and show more gait variability especially during dual-task conditions.[7,8] Different gait parameters, such as gait speed, step length, cadence, joint angles, and ground reaction forces, are dissimilar in diabetic patients compared with those with DSP.[8-10] Compared with normal walking, dual-task conditions affect all gait parameters in elderly diabetic patients. Additional analyses in elderly adults with diabetes show that those with impaired cognitive function walk more slowly, take shorter strides, have a shorter double-support time, and a greater variety in gait compared with those with an intact cognitive function.[8,11]

The purpose of this study was to examine the effectiveness of the application of analyzing treadmill, muscle strengthening, and balance training compared with a standard care intervention in patients with diabetic neuropathy, focusing the attention, primarily, on gait performances and, secondarily, on general functionality, cardiorespiratory parameters, and metabolic condition.

Methods

Design

We conducted a double-blind, randomized trial. Informed consent was obtained from all participants, and procedures were conducted according to the Declaration of Helsinki. The protocol (no. U0074917/11110) was approved by the Ethics Committee of Bergamo, Italy. The study has been registered at Trial Registration Current Controlled Trials website: NCT01926522.

Participants

A sample size calculation was performed to determine the necessary number of patients needed for this study based upon the results of a previous pilot study. Thirty-six patients, aged 45 to 90 years, were recruited for the study from August to September 2013. All patients had DSP-associated type 2 diabetes mellitus. Diagnosis was based on a clinical evaluation, in compliance with Diabetic Neuropathy Index criteria,[12] monofilament tests, and toe vibration executed by an expert diabetologist physician (FV with 8 years experience in this test).[13] Each patient underwent subjective and physical examination performed by a physician experienced in musculoskeletal problems and rehabilitation to evaluate inclusion and exclusion criteria. Patients were asked not to take analgesics, muscle relaxants, or anti-inflammatory drugs for 24 hours before the examination.

To be included in the study, the patients needed to have type 2 diabetes mellitus for greater than 3 years, (ie, the time from the diagnosis or the beginning of the first related signs or symptoms),[14] a diagnosis of DSP associated, and were able to walk autonomously.

Patients were excluded if they scored less than 5 points on the Functional Independence Measure (FIM)[15] locomotion scale, they showed articular ankyloses, contractures, spasms with locomotion effects, bone instability affecting lower limb functionality (unconsolidated fractures, vertebral instability, and severe osteoporosis), any clinicopathologic conditions contraindicating the rehabilitation treatment (respiratory insufficiency, cardiac/circulatory failure, osteomyelitis, phlebitis, and other conditions), cutaneous lesions at lower limbs, less than 22 points on the Mini Mental State Examination,[16] and any behavioral diseases involving aggressiveness or psychotic disorders.

None of the individuals in this study had received prior interventions for DSP. Therefore, they were unaware which treatment they received.

Outcome Measures

Primary Outcomes: Gait Performances. Various assessment tools were used to determine the motor abilities of the patients. All evaluation procedures were performed by the same examiner who was blinded to the aims of the study and to which group the patients were allocated. The 6-minute walk test (6MWT)[17,18] and 10-meter walking test (TWT)[19] were used to assess endurance and speed, respectively.

The 6MWT[17] quantifies functional mobility based on the distance in meters traveled in 6 minutes with interrater reliability estimated to be high (intraclass correlation coefficient, 0.90).[20] This outcome is a measure of endurance and is particularly significant to evaluate the possibility to perform continuative tasks that are particularly important for the rehabilitation of diabetic patients and are relevant for an autonomous life.[21]

The speed is quantified by the TWT over the ground.[19] The gait speed measurement is performed over the middle 6 meters of the TWT, and patients are asked to walk at their comfortable speed.[22] The interrater reliability of data is obtained with the TWT in patients with neurologic conditions (intraclass correlation coefficient, 0.93).[20] The combination of 6MWT and TWT are considered to evaluate the gait performances of the patients. Patients were instructed to walk as far as possible in 6 minutes; they could slow down and rest if necessary, but at the end of the test, patients should aim to not have been able to walk any further in the period. Subjects were informed at the halfway point (3 minutes) and when there was 1 minute to go.[23]

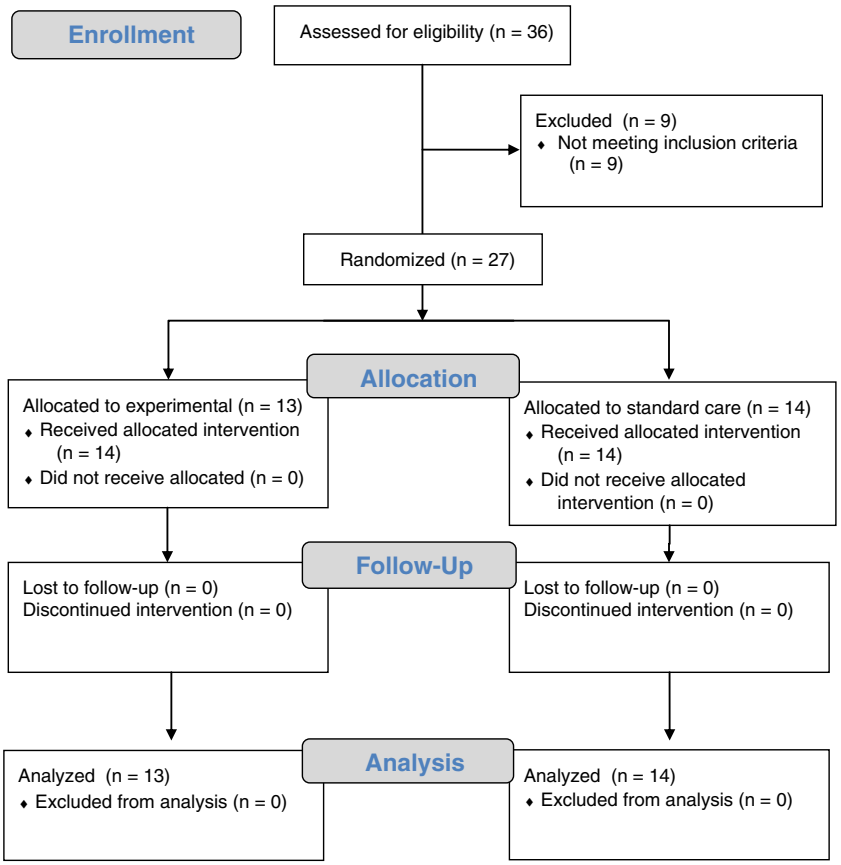

Fig 1. *Flow diagram of criteria in the study.*

Secondary Outcomes: Functional, Cardiac Respiratory, and Metabolic Tests. Afterwards, patients underwent the following functional tests:

- FIM that assesses severity of patient disability and medical rehabilitation functional outcome[15] and
- Tinetti scale that measures gait and balance abilities.[24]

Patients underwent the following cardiac respiratory measurements:

- Resting Energy Expenditure (REE), the amount of energy required for a 24-hour period during resting conditions;[25]
- Respiratory rate (RR), the number of breaths taken within 60 seconds;[26]
- Heart rate (HR), number of heartbeats per unit of time;[27]
- Oxygen saturation, (Spo_2) (%);[28]
- Maximal oxygen consumption, (Vo_2max);[29]
- Expired minute volume, (V_E) (L/min);[30]
- Fraction of expired air that is oxygen, (FEo_2) (%);[31]
- Systolic blood pressure (SBP); and
- Diastolic blood pressure (DBP).

Patients underwent the following metabolic measurement:

- Glycated hemoglobin (HbA1c) that is related to the average plasma glucose concentration over prolonged periods.[32]

All outcome measures were captured at baseline (pretreatment), immediately postintervention (posttreatment), and at 1-month postintervention by an assessor blinded to group assignment. The sequence of testing for the outcome measures was randomized among patients. The trial was designed according to the CONSORT publishing guidelines.[33]

Instruments

The computerized analyzer treadmill (Gait Trainer 3; Biodex, Shirley, NY)[34] is a rolling platform with pressure sensors able to calculate length, stride cadence, and the time in which the foot stays on the ground. The system gives a visual feedback with reference footprints, the distance of which is exactly the ideal length of stride for each patient. The patient can constantly check whether the length and

Table 1. *Baseline Demographics for Both Groups*

Basal Metabolic Data	Experimental (n = 13)	Standard Care (n = 14)	*P*
Age (y)	73 ± 10	71 ± 7	.52
Female, sex (n [%])	8 (61.5%)	9 (64.3%)	
Height (cm)	161.8 ± 8.2	158.0 ± 11.1	.3
Weight (kg)	77.1 ± 14.2	89.2 ± 27.0	.2
BMI	29.6 ± 5.9	35.3 ± 6.7	.03
Waist circumference (cm)	106.8 ±13.5	113.1 ± 15.7	.7
HR (beats per minute)	71.4 ± 9.8	70.5 ± 11.1	.4
RR (breaths per minute)	18.5 ± 4.0	19.1 ± 3.5	.3
Spo_2 (%)	95.2 ± 1.7	95.6 ± 2.6	.35
Vo_2max	201.6 ± 70.7	236.3 ± 64.0	.35
FEO_2 (%)	17.9 ± 1.0	16.6 ± 0.4	.35
HbA1c	8.8 ± 1.9	8.5 ± 1.5	.4
Fructosamine	196.2 ± 121.7	229.1 ± 157.6	.7
VE (L/min)	7.3 ± 2.2	7.4± 1.9	.7

Data are expressed as means ± SD.
BMI, body mass index; *FEO_2*, fraction of expired air that is oxygen; *HBAlc*, glycated hemoglobin; *HR*, heart rate; *REE*, resting energy expenditure; *RR*, respiratory rate; *Spo_2*, oxygen saturation; *VE*, expired minute volume; *Vo_2max*, maximal oxygen consumption.

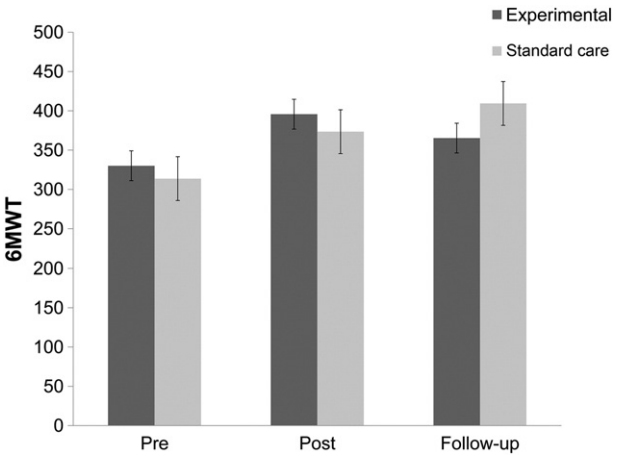

Fig 2. *Changes with experimental and standard care treatment. Results of the 6MWT initial values pretreatment, posttreatment, and follow-up. Data are expressed as mean ± SD.*

symmetry of the gait are regular and can properly control and optimize the movement.[35,36] Distal sensorimotor polyneuropathy patients show a reduced gait speed and an asymmetric gait, thus a device, especially able to work at low speed is interesting.

The Biodex System 4 (Biodex), is an electromechanical dynamometer, that is, a robotic device able to assist the patient during active or passive movements,[37] which enable walking even in case of reduced residual motor ability. Initially, the dynamometer can be set with constant speed (isokinetic mode), constant resistance (isotonic mode), or constant position (isometric mode). The Biodex Balance static and dynamic strengthening platform is a device, which gives information regarding the position of the projection of the barycenter to the ground with respect to the support base. This information may be detected statically, as movement of the barycenter projection within the support base or in a dynamic mode, as shift of the support surface with respect to the horizontal line. The dynamic mode allows users to adjust resistance of the ground to movements, thus giving patients a high-proprioceptive sensory stimulation. In the feedback of the device, users may visualize the ideal position and generate very accurate and stimulating motor tasks.

Randomization

After the completion of all baseline measurements, using a computer program (http://www.graphpad.com/quickcalcs/randomize1.cfm), patients were randomly assigned by an external assistant into 1 of 2 groups: experimental group or standard care group.

Multimodal Treatment Intervention

Patients in the experimental group received a multimodal treatment intervention consisting of 20 minutes of analyzing treadmill with feedback focused on symmetry and length of stride, 20 minutes of isokinetic dynamometric muscle strengthening of flexor and extensor muscles of tibiotarsal joint, and 20 minutes of balance retraining on dynamic balance platform. Each patient received 20 sessions over a period of 4 weeks (5 sessions per week).

Treadmill. The length of stride of reference that patients used as an aim during the exercise was personalized and depended on the height of patients.[34] Each patient carried out the feedback for 20 minutes with the aim of generating the most symmetric and regular gait. If the gait became sufficiently symmetric/regular, the patient was asked to increment the gait speed to improve the endurance. The inclination was always 0°.

Dynamometer. Patients using the dynamometer worked on strengthening flexor and extensor muscles with ankle speeds at 90°/s and 120°/s.[38] The strengthening technique was performed twice for 10 minutes each time with a 1-minute rest between sets.

Dynamic Balance Platform. The patient completed the retraining circuit undergoing a 20-minute feedback on dynamic balance platform by carrying out exercises in which they need to reach randomly appearing targets.[39] Patients began with 12 minutes the first 4 sessions, progressed to 16 minutes the next 2 sessions, then 18 minutes (2 sessions), and finally 20 minutes, if able, during the last 4 sessions. The level of difficulty of balance exercises is associated with the platform stiffness (maximum is 8 and minimum is 1). The balance training is most difficult with the least stiffness to tilting and is thus the least stable. The foot position was set with a preformed trapezoid

Table 2. *Mean (SD) for Outcome at All Study Visits for Each Group, Mean (SD) Difference Within Groups, and Mean (95% Confidence Interval) Difference Between Groups*

	Groups						Difference Within Groups						Difference Between Groups		
	Pretreatment		Posttreatment		Follow-up		Posttreatment minus pretreatment		Follow-up minus pretreatment		F − *P*		Pretreatment	Posttreatment	Follow-up
Outcome	Exp (n = 14)	SCG (n = 13)	Exp (n = 14)	SCG (n = 13)	Exp (n = 14)	SCG (n = 13)	Exp	SCG	Exp	SCG	Exp	SCG	Exp minus SCG	Exp minus SCG	Exp minus SCG
6MWT	330.1	313.8	395.7	373.5	6.2	5.4	65.6	59.8	35.2	59.8	6.547	3.712	16.3	22.2	−44.1
	(151.1)	(102.9)	(111.6)	(112.1)	(1.9)	(1.7)	(23.3)	(26.1)	(23.0)	(26.1)	(0.009)	(0.049)	(−117, 149)	(−90.2, 134.6)	(−173, 85.0)
SS	118.1		2190		8634										
F	0.068		0.175		0.524										
P	.8		.7		.5										
TWT	0.82	0.86	0.88	1.05	0.89	0.84	0.055	0.186	0.067	−0.016	0.396	1.509	−0.04	−0.17	0.47
	(0.3)	(0.2)	(0.4)	(0.5)	(0.4)	(0.4)	(0.94)	(0.105)	(0.119)	(0.133)	(0.68)	(0.253)	(−0.3, 0.3)	(−0.6, 0.3)	(−0.3, 0.4)
SS	0.006		0.124		0.01										
F	0.059		0.714		0.071										
P	.8		.4		.8										
FIM	116.4	117.0	119.3	120.9	118.0	121.0	2.90	3.88	1.600	4.500	6.970	7.532	−0.6	−1.6	−3.5
	(7.2)	(5.8)	(5.6)	(5.4)	(7.3)	(5.4)	(0.865)	(0.967)	(0.846)	(0.038)	(0.007)	(0.005)	(−7.3, 6.01)	(−7.1, 4.0)	(−10.0, 3.0)
SS	1.6		11.0		54.4										
F	0.036		0.361		1.29										
P	.9		.6		.3										
Tinetti scale walk	9.7	9.9 (1.9)	11.4	10.4	10.6	11.0	1.7	0.5	0.9	1.1	2.462	3.335	−0.2	1.0	−0.4
	(1.9)		(3.4)	(2.0)	(2.0)	(1.9)	(0.23)	(1.00)	(0.14)	(0.08)	(0.119)	(0.063)	(−2.1, 1.8)	(1.9, 3.9)	(−2.3, 1.5)
SS	0.136		4.669		0.711										
F	0.037		0.556		0.195										
P	.9		.5		.7										
SBP	141.7	152.3	143.9	143.9	149.4	148.1	2.222	−5.750	7.778	−4.125	1.105	0.242	−1.8	−3.5	3.6
	(13.0)	(20.3)	(24.7)	(23.7)	(6.4)	(17.4)	(1.000)	(1.000)	(0.568)	(1.000)	(0.358)	(0.788)	(−12.9, 9.3)	(−18.7, 11.5)	(−11.5, 18.7)
SS	474.4		28.9		7.373										
F	1.681		0.049		0.045										
P	.2		.8		.8										
DBP	82.2	79.8	81.7	82.8	81.9	79.0	−0.556	3.000	−0.333	−0.750	0.007	0.315	2.4	−1.1	2.9
	(9.7)	(12.2)	(16.2)	(7.0)	(12.5)	(12.8)	(4.592)	(4.870)	(3.711)	(3.936)	(0.993)	(0.735)	(−8.9, 13.8)	(−14.3, 12.1)	(−10.2, 16.0)
SS	25.9		4.97		35.3										
F	0.216		0.031		0.220										
P	.6		.9		.6										

RR (breaths/min)	25.7	29.9	26.1	31.1	26.1	32.1	0.400	1.250	0.400	2.250	0.030	1.171	−1.3	−0.5	0.5
	(7.4)	(4.8)	(4.8)	(5.4)	(6.1)	(6.7)	(1.000)	(1.000)	(1.000)	(0.696)	(0.970)	(0.337)	(−4.6, 1.9)	(−1.9, 0.9)	(−0.9, 1.9)
SS	77.5		112.2		161.3										
F	1.87		4.34		3.97										
P	.2		.05		.06										
HR (beats/min)	94.2	94.5	87.4	99.5	96.8	103.0	−6.8	5.0	2.6	8.5	0.699	1.564	−0.3	−12.1	−6.2
	(15.8)	(21.6)	(34.6)	(21.1)	(13.0)	(20.6)	(0.802)	(1.000)	(1.000)	(0.408)	(0.512)	(0.241)	(−19.0, 18.4)	(−41.7, 17.5)	(−23.1, 10.7)
SS	0.40		650.7		170.8										
F	0.001		0.751		0.608										
P	1		.4		.4										
Spo_2 (%)	93.8	96.6	97.3	96.1	94.8	96.8	3.556	−0.500	1.00	0.125	11.177	0.179	−2.8	1.2	−2.0
	(3.2)	(1.5)	(1.7)	(1.6)	(6.6)	(1.2)	(0.001)	(1.000)	(1.000)	(1.000)	(0.001)	(0.838)	(−5.5, -0.2)	(−0.5, 3.0)	(−7.0, 3.1)
SS	34.3		6.18		16.5										
F	5.397		2.163		0.692										
P	.04		.2		.4										
Vo_2max	754.3	985.6	746.8	717.8	797.6	1014.9	−7.519	−267.8	43.26	29.29	0.366	0.921	−231	29.0	−217
	(154.4)	(628.9)	(143.1)	(362.2)	(128.5)	(673.9)	(1.000)	(0.593)	(1.000)	(1.000)	(0.699)	(0.420)	(−666, 203)	(−235, 293)	(−676, 241)
SS	237,772		3728		209,909										
F	1.28		0.05		1.01										
P	.3		.8		.3										
REE	1509.7	1509.3	1392.7	1625	1634.3	1533.7	−117	116	125	24	0.688	0.205	0.4	−232	101
	(506.1)	(402.3)	(322.0)	(279.3)	(643.8)	(781.3)	(1.000)	(1.000)	(1.000)	(1.000)	(0.518)	(0.817)	(−466, 467)	(−538, 73.3)	(−611, 812)
SS	0.9		240,095		44,983										
F	0.00		2.6		0.09										
P	1.0		.13		.8										
V_E (L/m)	6.306	6.387	7.212	6.963	6.584	6.676	0.906	0.576	0.278	0.289	0.574	0.231	−0.08	0.249	−0.092
	(1.131)	(0.956)	(0.712)	(0.601)	(0.593)	(0.501)	(1.000)	(1.000)	(1.000)	(1.000)	(0.583)	(0.798)	(−3.38, 3.22)	(−1.83, 2.33)	(−1.82, 1.64)
SS	0.019		0.181		0.025										
F	0.003		0.072		0.014										
P	1		.8		.9										
F_{EO_2} (%)	16.925	17.135	17.418	16.805	16.735	17.117	0.493	−0.330	−0.190	−0.018	1.916	0.823	−0.21	0.613	−0.382
	(0.343)	(0.280)	(0.186)	(0.152)	(0.450)	(0.368)	(0.564)	(0.814)	(1.000)	(1.000)	(0.217)	(0.478)	(−0.81, 1.23)	(0.058, 1.167)	(−1.72, 0.959)
SS	0.106		0.900		0.350										
F	0.225		6.489		0.431										
P	.6		.03		.5										

6MWT, 6-meter walking test; *DBP*, diastolic blood pressure; *Exp*, experimental group; *F*, F ratio; F_{EO_2}, fraction of expired air that is oxygen; *FIM*, functional independence measure; *HR*, heart rate; *REE*, resting energy expenditure; *P*, statistical significance; *RR*, respiratory rate; *SBP*, systolic blood pressure; Spo_2, oxygen saturation; *TWT*, 10-meter walking test; *VE4*, expired minute volume; Vo_2max, maximal oxygen consumption; *SCG*, standard care group; *SS*, sum of squares.

(heels at 20 cm distance with feet forming an angle of 20°). For safety purposes, the patients were permitted to touch handrails trying to avoid using them as a help. The patient was asked to perform bilateral exercises that begin with static level and progress to dynamic level.[1] A measurement of the patient performances is the length of the route to the target and the time to gain the target.

Standard Care Intervention

Patients in the standard care group received the same number of treatment sessions of a similar duration as those in the experimental group, but they received activities targeted to improve the endurance, manual exercises of lower limb muscle strengthening, and stretching exercises, in substitution of the robotic treadmill and dynamometer (ie, sitting to standing, walking up and down a slope, and stair climbing). Gait retraining on the floor for 20 minutes and static and dynamic balance exercises in upright position in substitution of the dynamic balance platform training (ie, stance on heel/toes, tandem stance, one leg stance, and different kinds of walking).

Protocol

The patients in both groups were treated by a clinician with postgraduate orthopedic physiotherapist training and more than 8 years of clinical experience in the management of musculoskeletal disease. The physical therapist was blinded to all data that were collected for the study. The patients were assigned to experimental and standard care treatment groups with simple randomization. All patients received 20 treatment sessions scheduled on separate days, at least 24 hours apart and at the same time of day, 5 days per week, for 4 weeks. All outcomes were collected by an external assessor blinded to the treatment allocation of the participants.

Statistical Analysis

Data were analyzed using SPSS version 19.0 (SPSS Inc, Chicago, IL), conducted after an intention-to-treat analysis using the last value forward method. Normal distribution of the sample was analyzed using the Kolmogorov-Smirnov test ($P < .05$). The Student t test was used to analyze the 6MWT and TWT measurements, comparing the experimental group with the standard care group data. A 2 × 2 repeat measures analysis of variance (ANOVA) was used, and the factors analyzed were time (pretreatment and posttreatment) and group (treatment and standard care group) interaction. The Bonferroni test was used for the post hoc analysis of specific comparisons between variables. When the differences were not significant with ANOVA, the post hoc was not performed, and the statistical analysis, finished. Correlation coefficient's values assumed weak (<0.3), moderate (0.3-0.6), and strong (>0.6).[40] The Spearman rank correlation coefficient (Rs) was used to evaluate the relationship between the 6MWT distance and the other parameters evaluated. The Spearman rank correlation coefficient values were interpreted according to Domholdt recommendations.[41] The statistical analysis was conducted at a 95% confidence level, and a $P < .05$ was considered statistically significant.

Results

Thirty-six consecutive patients (n = 36) with DSP, a variant of diabetic neuropathy, were screened for eligibility criteria. Twenty-seven patients (mean ± standard deviations (SD) age, 72 ± 9 years; 63% female) satisfied all eligibility criteria, agreed to participate, and were randomized to the standard care (n = 14) or experimental (n = 13) groups. The reasons for ineligibility were nonindependent gait (n = 5), medically instable (no uncontrolled hypertension and arrhythmia) (n = 2), no confirmation of the diagnosis with neurologist (n = 1), and the concurrent presence of pneumonitis (n = 1). Figure 1 provides a flow diagram of subject recruitment and retention through the study. Baseline features of both groups were similar for all variables (Table 1). No adverse effects were detected during or after the application of the treatment, and none of the patients started drug therapy during the study (Fig 2).

Primary Outcomes: Gait Performances

6-Minute Walk Test. The 2 × 2 repeated ANOVA revealed a significant effect of time ($F_{[2.0]} = 9.636$; $P = .001$; partial $\eta = 0.4$) but not for the group × time interaction ($F_{[2.0]} = 2.369$; $P = .11$; partial $\eta = 0.129$) in 6MWT. The post hoc analysis revealed significant differences between the 20 sessions for the experimental group ($P = .001$) but not for the standard care group. In addition, the 6MWT increased after the intervention, and the major difference was found at the follow-up ($P = .005$) for the standard care group. There was no significant difference between the groups ($P > .05$). Between-group effect size was weak ($d = 0.2$) after the intervention and weak to moderate ($d = 0.35$) at follow-up period. The data are summarized in Table 2.

10-Meter Walking Test. For speed measured over the TWT, there was no significance for time ($F_{[2.0]} = 0.852$; $P = .436$; partial $\eta = 0.051$) or group × time ($F_{[2.0]}$, 0.616; $P = .546$; partial $\eta = 0.037$) interactions (Table 2). Between-groups effect sizes were weak at posttreatment and follow-up periods ($d < 0.2$).

Secondary Outcomes: Functional, Cardiac Respiratory, and Metabolic Tests

Outcome for FIM demonstrated a significant time factor ($F_{[2.0]} = 9.708$; $P = .001$; partial $\eta = 0.38$). All participants in both groups demonstrated changes (increases) over the month. The group-by-time interaction was not significant ($F_{[2.0]} = 1.518$; $P = .235$; partial $\eta = 0.087$). We found significant differences between the pretreatment and

Table 3. *Spearman Rank Correlation Coefficients Between the 6MWT Distance and the Other Parameters*

Basal Metabolic Data	Spearman *r*	*P*
Age	−0.14	.47
Height	0.39	.04
Weight	−0.008	.97
BMI	−0.25	.2
Waist circumference	−0.26	.19
SBP	−0.43	.03
DBP	−0.17	.4
HR*	−0.14	.49
Respiratory rate	0.08	.69
Spo_2	0.17	.39
Vo_2max	0.023	.91
Feo_2	0.468	.01
HbA1c	−0.44	.06
Fructosamine	0.006	.98
V_E	0.041	.84
REE	0.061	.76
TWT	0.62	.001
FIM	0.646	<.001
Tinetti scale	0.596	.001

BMI, body mass index; *DBP*, diastolic blood pressure; *FIM*, functional independence measure; *HR*, heart rate; Feo_2, fraction of expired air that is oxygen; *HBAlc*, glycated hemoglobin; *REE*, resting energy expenditure; *SBP*, systolic blood pressure; Spo_2, oxygen saturation; *TWT*, 10-meter walking test; V_E, expired minute volume; Vo_2max, maximal oxygen consumption.

posttreatment periods in the experimental and standard care group (all, $P < .01$). We found that the standard care group caused significant differences between pretreatment (117.0 ± 5.8) and follow-up period ($P = .04$).Regarding the results of the Tinetti scale, SBP, DBP, RR, heart rate, Spo_2, REE, Vo_2max, V_E, and Feo_2, the 2×2 repeated ANOVA revealed a not significant effect of time and group × time interaction.

Spearman rank correlation coefficients showed a strong, significant, and positive relationship between the 6MWT distance and the TWT, FIM, and Tinetti scale ($r_s = 0.62$, 0.646, and 0.596, respectively, all $P = .001$) and a significant, moderately strong, positive relationship between the 6MWT distance and the height, Feo_2 and SBP ($r_s = 0.47$, $P = .01$; $r_s = 0.39$, $P = .04$; and $r_s = 0.43$, $P = .03$, respectively). No significant correlation was found between the 6MWT distance and weight, body mass index (BMI), waist circumference, SBP, DBP, HR, RR, Spo_2, Vo_2max, HbA1c, fructosamine, V_E, and REE. Finally, a moderately strong, significant, positive correlation was found between the TWT and the FIM and Tinetti scale ($r_s = 0.435$, $P = .02$ and $r_s = 0.431$, $P = .03$), (Table 3).

Discussion

This randomized clinical trial examined the effects of a treatment analyzing treadmill, muscle strengthening, and balance training on a patient population with DSP at short-term follow-up. The results demonstrated that patients receiving a multimodal intervention including analyzing treadmill with feedback focused, isokinetic dynamometric muscle strengthening, and balance retraining on dynamic balance platform exhibited significantly greater improvements on the gait endurance after 4 weeks of treatment compared with those who received a standard care intervention, whereas they do not produce significant improvements of the gait speed. It is interesting to note that both the treatments produce a significant improvement of functionalities (FIM) of the patients but not in the cardiac respiratory and metabolic tests; one result was statistically significant in Spo_2 but not clinically (all values were above 90%). We believe that these results are interesting because they help focus on different aspects of the patients with DSP, in general but especially in relation to the walking ability. We believe this provides evidence to support the use of this multimodal approach in patients with DSP.

Diabetes may cause limited joint mobility of both small and large joints, a condition known as cheiroarthropathy, that can result in an impairment of many daily activities. Gomes et al[42] have shown that, when diabetic individuals face a new challenging situation that induces a higher demand for muscle strength and propulsion, the necessary range of motion and neuromuscular control around distal joints are insufficient. Furthermore, DSP decreases muscle strength[43] is highly associated with walking performances also without manifest mobility limitations. Distal sensorimotor polyneuropathy patients are at high risk for foot ulceration[44] and plantar skin breakdown due to unnoticed plantar stresses during walking,[44,45] risk of falling due to a very small change in postural stability in elderly[46], and a neuropathic pain that contributes to gait variability; these causes patients to decrease the capacity of walking. We did observe differences endurance values between both groups. Numerous studies have shown interventions directed to the gait to exert an endurance effect by increasing the distance.[47,48] The increase in gait endurance over the patients immediately postintervention are consistent with the results by Allet et al,[49] who showed that gait training and balance exercises for twice a week for 60 minutes in patients with diabetes had an immediate endurance effect. These techniques are frequently performed and are often included as an integral part of the rehabilitation program.[50]

In contrast to the differences between groups for gait endurance, there was no difference between groups for gait speed, cardiac respiratory, and metabolic tests after the intervention. The current study was powered to detect changes in gait as measured by the gait endurance and not gait speed. Potentially, a larger sample size may have detected significant changes in gait speed between groups. The gait speed is related with the life expectancy,[51] whereas the endurance is related with life quality[52] as confirmed by our results (FIM). This result can be associated to the type of rehabilitation program that is more devoted to endurance than to gait speed and probably to the reduced follow-up period limited to 1 month. Previous studies examining the effects of gait,[53] in these different populations indicated a

dissimilarity between groups for gait speed measurements. However, in these studies, the differences in gait speed did not exceed the SD and thus were within measurement error and likely not clinically meaningful. But, our findings are similar to the results of a study performed on early after-stroke patients in which patients who received (18 treatments) did not exhibit changes in gait speed different from those receiving a control intervention, whereas showing significant differences in the endurance improvement.[54] However, as the authors reported, this might be the result of differing patient expectations, which were not measured in the current study. The experimental program has been adopted for different pathologies, that is, poststroke rehabilitation,[55] traumatic brain injury,[56] and incomplete spinal cord injury.[57]

Limitations and Future Studies

There are a number of limitations to this study that must be considered. We did not use a pain outcome measure, which would have provided an indication as to the effectiveness (or lack) of the current treatment approach for improving function in individuals with neuropathy. In addition, because only one therapist performed all interventions, generalizability of the results may be limited. Follow-up period was limited to 1 month, and therefore, we cannot be certain if the gait endurance improvement lasted beyond that time. The patients all received the same standard treatment and may have been either overtreated or undertreated as a result without specifically addressing impairments unique to each patient. Future randomized clinical trials should be conducted using multiple therapists, include a measure of function, and collect data at a long-term follow-up. An interesting of this work limitation is the focus only on the gait as a single task; patients with DSP show important difficulties in dual-task activities, that is, walking and talking or walking and carrying a cup of water. We decided to limit the study to a single task, but a complete treatment of DSP patients should take care of dual-task activities in the training phase and also in the measurement phase. For this reason, further developments must focus also on this issue.

Future studies should include further in-depth analyses that are necessary in comparing the 2 groups with an increment of enrollments and of secondary outcomes focusing the attention on the possibility of finding indications and contraindications.

Conclusion

The study results suggest that the rehabilitation program may show positive effects on the gait endurance after 4 weeks of treatment, whereas it did not produce significant improvements of gait speed. Both treatments produced a significant improvement of functionalities for the patients in this study.

Practical Applications

- The experimental rehabilitation program showed positive effects on gait endurance after 4 weeks of treatment.
- The experimental rehabilitation program did not produce significant improvements of gait speed.
- Both treatments produced a significant improvement of functionalities for the patients in this study.

Funding Sources and Potential Conflicts of Interest

No funding sources or conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): G.T, JHV, F.V, C.L, A.B, S.N.
Design (planned the methods to generate the results): G.T, F.V, C.L, A.B.
Supervision (provided oversight, responsible for organization and implementation, and writing of the manuscript): G.T, JHV, F.V, C.L, A.B, S.N.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): G.T, F.V, C.L, A.B.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): G.T, JHV, F.V, C.L, A.B, S.N.
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Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): G.T, JHV, F.V, C.L, A.B, S.N.

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