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Original article

Co-contraction of lower limb muscles affects gait stability in patients with diabetic peripheral neuropathy

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ABSTRACT

【Background/Purpose】Patients with diabetic peripheral neuropathy (DPN) experience an increased risk of falls and decreased quality of life due to impaired balance and gait. This study aimed to identify factors associated with gait instability in DPN patients.

【Methods】Forty DPN patients (age: 58.8 ± 9.3 years; 16 males, and 24 females) admitted to our hospital for diabetic education were included in the study. The instability in gait was assessed using a triaxial accelerometer, which was affixed to the third lumbar spinous process reflecting the center of gravity. The root mean square (RMS) value was calculated from the data acquired during walking and corrected by the squared value of body weight. Electromyography was used to evaluate the co-contraction of lower leg muscles; the co-contraction index (CI) was calculated for the tibialis anterior and soleus muscles during walking. For each evaluation, data were obtained from a 10 m walk test at the patient's comfortable speed. Pearson's correlation analysis was used to study the relationship between each parameter. In addition, multiple regression analysis was conducted with RMS as the dependent variable and vibration perception, CI, maximum ankle dorsiflexion muscle strength, and maximum ankle plantarflexion muscle strength as independent variables. Moreover, multiple regression analysis was performed with RMS as the dependent variable, CI as the independent variable, and adjusted for age, gender, and height.

【Results】The results showed that RMS was significantly correlated with the CI of lower leg muscles ($\beta = 0.45$, $p < 0.01$). Further, this relationship remained significant even after adjustment for age, gender, and height ($\beta = 0.54$, $p < 0.01$).

【Discussion】These results suggest that co-contraction of the lower leg muscles affects the overall stability during walking in DPN patients.

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Introduction

The total number of diabetic patients increased from 108 million in 1980 to a significant 422 million in 2014[1]. In 2019, diabetes mellitus was the ninth leading cause of death, with an estimated 1.5 million deaths directly attributable to diabetes[2]. Diabetic peripheral neuropathy (DPN) affects more than half of all diabetic patients and is associated with particularly high morbidity[3]. In Japan, an estimated 35.8% of all individuals diagnosed with type I or type II diabetes develop DPN[4].

Patients with DPN experience an increased risk of falls and decreased quality of life because of impaired balance, posture, and gait[5,6]. The gait in DPN is characterized by a decrease in speed, step length, and cadence and an increase in the step variability, besides the prolonged stance period and support phase bilaterally[7-9]. These gait changes are more pronounced when walking on irregular surfaces[8,9]. DPN patients also reportedly have lower ankle moment and ankle power, and altered start-stop timing of muscle activity compared to healthy controls[10]. Additionally, a co-contraction of agonist and antagonist muscles of the ankle and knee joints is often observed in these patients during the stance phase. Older adults have a higher incidence of simultaneous lower leg muscle contractions during gait compared to younger adults[11], It is also known that reduced balance is associated with greater simultaneous lower limb muscle contractions[12]. Ge[13] explained that rigid body movements induced by excessive muscle contractions may increase the risk of instability in postural disorders. However, the effect of simultaneous lower limb contractions (co-contraction) on gait instability in DPN patients remains unclear. Clarifying the relationship between gait stability and simultaneous leg muscle contraction and ankle muscle strength in patients with DPN will be beneficial for the development of physical therapy treatments.

Therefore, the purpose of this study was to investigate the effect of co-contractions of the lower limb muscles on gait stability in patients with DPN. We hypothesized that simultaneous contraction of the lower leg muscles (tibialis anterior and soleus muscles) during gait would affect the patient's overall stability during walking. It is anticipated that this study will provide evidence of the cause of gait instability in DPN patients.

Methods

2.1 Participants

We recruited adult type 2 diabetic patients with DPN who were hospitalized at the Department of Endocrinology, International University of Health and Welfare, Atami Hospital. Those who were able to walk independently and had no significant cognitive impairment (Mini-Mental Status Examination score of 24 or higher) were included in the study. Patients were excluded if they had severe chronic heart failure, severe chronic renal failure, severe retinopathy,

current bilateral foot ulcers, neuropathic pain, malignancy, or were pregnant.

Those who agreed to participate in the study were contacted individually by the research collaborators for an appointment and provided written informed consent. The study complied with the principles of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the International University of Health and Welfare (Reg no - 16-Io-158). All subjects gave written and oral, informed consent prior to participation.

2.2 Clinical parameters assessment

Age, sex, comorbidities (hypertension, hyperlipidemia), and behavioral history (drinking and smoking history) were recorded from the medical records. Physical therapist measured the subject's height, weight and body mass index (BMI). Laboratory assessment was performed, including for hemoglobin A1c (HbA1c), Plasma glucose, low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (γ-GPT) and triglyceride (TG).

2.3 Sensory neuropathy assessment

Diabetic neuropathy was diagnosed following the simplified diagnostic criteria proposed by the Diabetic Neuropathy Study Group in Japan[14] based on the presence of two of the following three factors: 1) subjective symptoms in bilateral lower limbs or feet; 2) absent or reduced bilateral Achilles tendon reflex; 3) decreased vibration perception – assessed using a C-128 tuning fork and measured bilaterally at the medial malleoli.

2.4 Assessment of gait parameters

All participants wore their normal shoes and were asked to walk along a 10-m path (with 3 m provided for acceleration/deceleration) set up in a corridor with a flat floor at a speed of their choice. The walking speed (in m/sec) was calculated by dividing the distance (10 m) by their walking time (in seconds). Stride length was calculated from the number of steps taken during the 10 m, and cadence was calculated from the walking time and the number of steps taken during the 10 m.

2.5 Assessment of gait instability

A triaxial accelerometer (TSND121, ATR-Promotions Inc, Japan) was firmly fixed with a band to position it at the third lumbar spinous process, which reflects the body's center of gravity in the standing position. Data were measured for acceleration in the mediolateral (ML), vertical (V), and anterior-posterior directions during the 10-m walk at the patient's preferred speed[15]. The sampling frequency was set to 200 Hz and data were sent to a PC in real-time via Bluetooth to be read by a data acquisition software, SensorController (ATR-Promotions Inc., Japan), and then recorded as a.csv file. After signal correction, the root-mean-square (RMS) values for each direction were calculated using the following equation[16].

$$RMS = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N}(x_i)^2}}{v^2}$$

RMS is a statistical measure of the magnitude of acceleration in each direction. Menz et al[15]. reported that the RMS demonstrated a non-linear relationship to walking speed; therefore, the RMS values were

normalized by the square of the walking speed.

2.6 Assessment of co-contraction

Surface electromyography (EMG) using the TeleMyo G2 – EM-601 equipment (NORAXON Inc., USA) was recorded for two muscles, tibialis anterior and soleus, using active electrodes (BlueSensor M-00-S, Ambu, Denmark) that were attached by lightly rubbing the skin of each muscle belly. The electrodes were placed carefully so that the innervated zone was not sandwiched between two electrodes, and to minimize crosstalk from adjacent muscles.

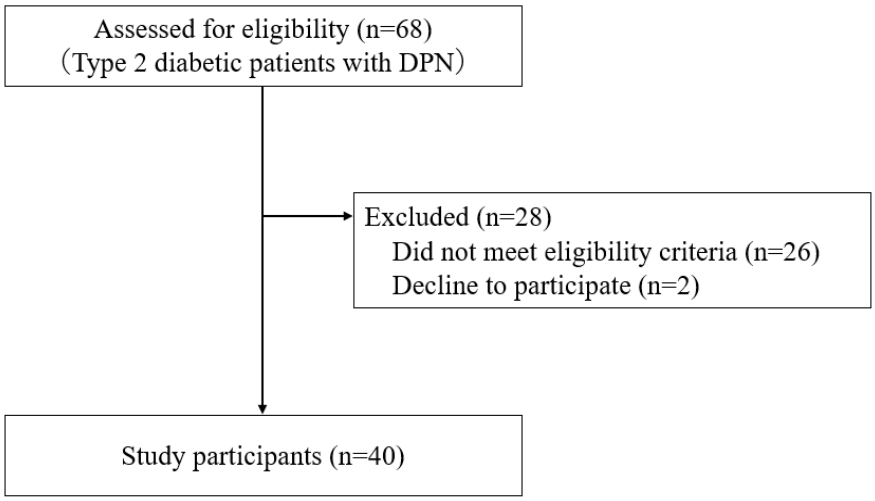

Figure 1. Flow chart of the patients participated in the study.

The sampling frequency was set at 1500 Hz. The EMG signals were filtered with a band-pass filter (passband: 20–500 Hz) to remove noise and then recorded on a disk. The gait cycle was defined by successive foot contacts with signals from a footswitch (EM434, NORAXON Inc., USA). The EMG data were rectified and interpolated to 100 equally-spaced values each time the foot contact activated the footswitch. All linear envelope values were then normalized by the peak activation during walking[17]. To measure the co-contraction of antagonistic muscles, the ratio of activation between tibialis anterior and soleus muscles (TA/SOL) was calculated. The co-contraction index (CI) was calculated using the following formula given by Falconer et al[18]:

$$I_{\text{ant}} = \int_{t1}^{t2} EMG_{TA}(t)dt + \int_{t2}^{t3} EMG_{SOL}(t)dt$$

$$I_{\text{tortal}} = \int_{t1}^{t3} [EMG_{agon} + EMG_{ant}](t)dt$$

$$CI = \frac{2Iant}{I_{tortal}} \times 100\%$$

2.7 Ankle plantar-dorsiflexion muscle strength measurements

A Biodex® system-3 isokinetic dynamometer (Biodex

Medical Systems, Shirley, NY, USA) was used for measuring the peak torques of ankle dorsi-flexors and plantar-flexors. The test procedure was performed according to manufacturer guidelines. Each subject was placed in a semi-supine position with the knee and hip joints at 60 degrees. Each subject was instructed to perform a maximal isometric contraction of ankle plantarflexion and dorsiflexion starting from a neutral ankle joint position (at 0°). Three trials were performed for the measurements and the average values were calculated.

2.8 Statistical analysis

We used the Shapiro–Wilk test to confirm the distribution of the variables. Pearson's correlation analysis was used to study the relationship between each parameter. In addition, multiple regression analysis was conducted with RMS as the dependent variable and vibration perception, CI, maximum ankle dorsiflexion muscle strength, and maximum ankle plantarflexion muscle strength as independent variables.

Results

3.1 Participant characteristics

We screened 68 participants, of which 40 participants were selected for the study (age: 58.8 ± 9.3 years; 16 males, and 24 females) (Figure 1). The clinical characteristics of all participants are presented in Table 1.

3.2 Relationship between each parameter

The RMS value showed a significant negative correlation with vibration sense ($r = -0.39$, $p < 0.05$) and a significant positive correlation with CI ($r = 0.53$, $p < 0.01$), but no significant correlation with other parameters (Table 2). In addition to the result, vibration perception showed a significant positive correlation with ankle plantar flexion muscle strength ($r = 0.38$, $p < 0.05$) and a significant negative correlation with CI ($r = -0.39$, $p < 0.05$) (Table 2). Leg muscle strength showed a significant positive correlation with plantar flexion and dorsiflexion muscle strength ($r = 0.47$, $p < 0.05$), but no significant correlation with other parameters (Table 2).

Multiple regression analysis with RMS as the dependent variable showed a significant relationship only for CI ($\beta = 0.45$, $p < 0.01$) (Table 3). To further investigate the effect of CI on RMS, multiple regression analysis adjusted for age, sex, and body mass index (BMI) was performed, and CI was still significantly related to RMS ($\beta = 0.53$, $p < 0.01$) (Table 4).

Discussion

The purpose of this study was to investigate factors that influence gait stability in patients with DPN. We observed that gait instability was influenced by the simultaneous contraction of the leg muscles (tibialis anterior and soleus muscles) and this relationship did not change even when adjusted for age, gender, or BMI.

The gait of patients with DPN is characterized by an apparent decrease in speed, stride length, and cadence, along with an increase in the stance period and support of both limbs[7-9]. Additionally, patients with DPN tend to have greater gait instability than those without DPN[19], which can be attributed to persistent hyperglycemia and adipocyte accumulation, increasing oxidative stress, polyol metabolism, and inflammatory cytokines[20,21].

Table 1. Descriptive characteristics of the participants

	DPN (n = 40)
Physical	
Age (years)	58.8 ± 9.3
Sex (male/female)	16 /24
Height (m)	1.62 ± 0.09
Weight (kg)	69.4 ± 20.3
BMI (kg/m^2)	26.3 ± 5.6
Diabetic neuropathy symptoms	
Duration of DM (years)	6.8 ± 8.2
Vibration perception (s)	8.14 ± 2.0
Subjective symptoms (n)	7 (17.5%)
Absent or reduced ankle jerk (n)	28 (70.0%)
Duration of DM (years)	6.8 ± 8.2
Insulin treatment (n)	4 (10%)
Complication	
Hypertension (n)	21 (52.5%)
Hyperlipidemia (n)	31 (77.5%)
Behavioral history	
Drinking history (n)	21 (52.5%)
Smoking history (n)	19 (47.5%)
Biochemistry	
HbA1c (%)	11.2 ± 2.0
Plasma glucose (mg/dl)	297.6 ± 7121.3
LDL-C (mg/dl)	124.9 ± 437.5
ALT (IU/L)	40.5 ± 30.3
γ-GPT (IU/L)	53.1 ± 343.3
TG (mg/dl)	188.7 ± 8162.9
Gait parameters	
Gait speed (m/sec)	1.26 ± 0.19
Step length (cm)	62.6 ± 8.2
Cadence (step/min)	122.5 ± 210.2
CI (%)	47.9 ± 11.4
RMS (m/s^2)	2.75 ± 0.49
Ankle strength	
Plantar flexion strength/weight (%)	111.4 ± 40.4
Dorsiflexion strength/weight (%)	35.7 ± 13.2

Values are mean ± standard deviation or number (%). DPN, diabetic peripheral neuropathy; BMI, body mass index; DM, diabetes mellitus; PPDR, pre proliferative diabetic retinopathy; LDL-C, low-density lipoprotein cholesterol; ALT, alanine aminotransferase; γ-GPT, gamma-glutamyl transpeptidase; TG, triglyceride; CI, co-contraction index; RMS, root mean square.

These factors cause inhibition of Na+/K+-ATPase activity, decrease in eNOS and NO, and decrease in micro-vascularity, resulting in a loss of peripheral nerve myelin sheath, axonal deformation, and decrease in sensory receptors[22,23]. This further reduces the intrinsic sensory feedback during movement and makes postural control difficult[24]. Najafi et al.[25] reported that gait variability and the coefficient of variation of gait speed were significantly higher in the DPN group when age-matched subjects and DPN patients walked barefoot both for short distances (7 m) and long distances (20 m). Furthermore, there was a high correlation between the severity of neuropathy and gait instability exhibited in barefoot walking/distance walking condition[25]. Brown et al.[26] reported that DPN patients have a greater lateral displacement of the center of mass from the center of foot pressure in planar gait than in patients without diabetes mellitus, requiring greater muscle activity to control posture. Moreover, patients with DPN having reduced peripheral nerve function have reduced ankle joint mobility during gait[27], altered coordination of the tibialis anterior and triceps femoris muscles, and increased muscle activity[10,28]. These abnormalities in muscle activity may contribute to the increased instability of gait.

Table 2. Relationship between each parameter

	RMS	Age	Height	Vibration perception	CI	Plantar flexion strength	Dorsiflexion strength
RMS	-	0.15	−0.83	−0.39*	0.53**	−0.22	−0.05
Age		-	−0.35*	−0.20	−0.17	−0.26	−0.06
Height			−	−0.19	−0.28	0.29	0.68**
Vibration perception				−	−0.39*	0.38*	0.19
CI					−	−0.12	−0.13
Plantar flexion strength						−	0.47*
Dorsiflexion strength							−

*< 0.05, ** < 0.01; RMS, root mean square; CI, co-contraction index.

Table 3. Multiple regression analyses of RMS and clinical parameters

	Unstandardized coefficients		Standardized coefficients	T	p-value	95% confidence interval for β	
	B	Std. error	Beta			Lower bound	Upper bound
Constant	2.314	0.590	-	3.919	0.000	1.115	3.512
CI	0.019	0.007	0.450	2.962	**0.005**	0.006	0.033
Vibration perception	−0.043	0.041	−0.179	−1.072	0.291	−0.126	0.039
Plantar flexion strength	−0.001	0.002	−0.089	−0.483	0.632	−0.006	0.003
Dorsiflexion strength	−0.001	0.008	−0.009	−0.053	0.958	−0.017	0.016

Adjusted R^2= 0.252

CI, co-contraction index

In this study, only the co-contractions affected gait instability. A study by Nagai et al.[12] showed that simultaneous contraction of lower limb muscles was higher in those with lower balance functions. Höhne et al.[29] reported that co-contractions in the lower limb during walking were affected by decreased sensory nerve function. Furthermore, Marques et al.[17] found that greater co-contractions in elderly subjects resulted in greater gait instability and higher walking costs. Co-contraction of muscles of the lower leg may occur as a strategy to increase joint stability to maintain balance; in DPN patients, it may be a strategy to compensate for the loss of balance caused by decreased sensory function. On the other hand, co-contraction may increase the stiffness of the joint, thereby decreasing the smoothness of gait and affecting the overall stability during walking.

Our results also showed that the maximal ankle plantar-dorsiflexion muscle strength did not have a significant relationship with gait instability. Manor et al.[30] investigated the causes of gait instability in normal subjects and DPN patients, and reported that muscle strength was related to gait instability in normal subjects; however, gait stability in DPN was related to standing balance and not muscle strength. The mean maximum muscle strength of our study sample was 111.4% ± 40.4% for ankle plantar flexion and 35.7% ± 13.2% for ankle dorsiflexion, which was lower than the average value for the same age group in another study consisting of healthy subjects[31]; however, the difference was small and may not have been enough to affect their gait.

Table 4. Multiple linear regression analysis to investigate the effects of CI on RMS after adjusting for age, sex, height.

	Unstandardized coefficients		Standardized coefficients	T	p-value	95% confidence interval for β	
	B	Std. error	Beta			Lower bound	Upper bound
Constant	0.944	2.484	−	0.380	0.706	−4.098	5.986
CI	0.023	0.006	0.541	3.651	**0.001**	0.010	0.036

Adjusted R^2= 0.216

CI, co-contraction index; RMS, root mean square.

There are several limitations to this study. First, the sample size was small, which could lead to type II errors, especially given the number of gait parameters that were investigated. Secondly, the study did not measure any index other than leg muscle activity for gait instability. Gait is influenced by many muscles attached across the lower limb, pelvis, and trunk. Notably, the thigh and hip musculature compensates for the reduced function of the lower legs and has a significant impact on the gait of a patient with DPN[32]. In addition, de Mettelinge et al.[33] found that elderly diabetics with impaired cognitive function had slower walking speed, shorter stride length, shorter double-support time, and greater gait variability compared to participants with normal cognitive function. Thus, regardless of neurological impairment, gait is significantly affected by cognitive decline. Future studies that investigate additional parameters that affect gait are needed.

Conclusions

The results of this study reveal that gait instability in DPN patients is affected by simultaneous contraction of the lower leg muscles, and this relationship is not influenced by the patient's age, sex, or BMI. Future studies should be conducted with a larger sample to include the evaluation of gait-related parameters and further investigate the causes of gait instability.

Conflict of Interest

There are no conflicts of interest to disclose for this study.

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