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Assessment and Trèatment of Gait in Diabetic Peripheral Neuropathy: A Focused Review of Evidence

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Abstract

Background: Walking is an integrated function of neurophysiological and musculoskeletal systems which in turn depends upon cardiorespiratory and metabolic systems for energy cost and expenditure. **Objective:** To evaluate the abnormalities of gait in patients with diabetic peripheral neuropathy (DPN) by reviewing studies on assessment and treatment. **Methods:** A systematic review of PubMed was done using search terms of diabetic neuropathy and gait for articles in English with abstracts and independent blinded data extraction and synthesis was performed to identify studies on assessment and treatment. **Results:** Reduced gait speed, reduced double support time, reduced step length, reduced ankle range of motion, with increased ankle invertor-evertor moment; altered plantar pressures with increased load under midfoot compared to rearfoot; earlier muscle activity of soleus, tibialis anterior, vastus medialis and medial hamstrings with delayed muscle activity of vastus lateralis and lateral gastrocnemius; longer loading time with decreased mediolateral and longitudinal center of pressure excursions were reported in gait of individuals with DPN. Gait-related interventions in DPN population studied were physiotherapy including walking prescription, lower extremity strengthening and balance exercises, footwear and insoles, and visual feedback which were shown to improve balance, gait speed, muscle activity and plantar pressures in this population. **Conclusion:** There were alterations in temporal and spatial gait parameters, muscle activation patterns, and loading time responses which is essential for clinicians examining patients with DPN, and interventions such as physiotherapy, footwear and insoles and visual feedback were reported to be useful to improve gait in people with DPN.

Keywords: Gait; Human walking; Bipedal locomotion; Diabetic neuropathy; Functional mobility.

Introduction

Human walking or gait had evolved phylogenetically and ontogenetically from quadupedialism to bipedalism to provide locomotion with advanced adaptive functions to suit the needs of the person, the task and the environment.[1] Walking is an integrated function of neurophysiological and musculoskeletal systems which in turn depends upon cardiorespiratory and metabolic systems for energy cost and expenditure.[2]

The human gait has temporal and spatial parameters measured using distance and time variables respectively, which gets altered in pathological states that affect the sensorimotor function of gait. The dynamics of human gait is well understood for its complexity in its response to stress and evolution[3] and the importance of measuring human gait in different medical conditions cannot be overemphasized.[4]

The role of spine and pelvis,[5] hip and thigh,[6] and knee[7] in the evolution and natural history of human gait is recognized for their relative segmental alignment and their dynamic interactions as a closed kinetic chain.

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The role of visual, vestibular and somatosensory systems in static and dynamic balance as well as during gait is essential in controlling the direction or trajectory of center of gravity in a three-dimensional and multidirectional motion.[8]

Studies on gait had previously focused on disorder-specific deviations,[9] methods or techniques of gait analysis,[10] and direction-specific deviations.[11] Changes in gait parameters such as shorter stride length, reduced walking speed, and altered lower limb and trunk mobility were previously reported in persons with diabetes mellitus (DM)[12] which were influenced by cognition, mood, lower-extremity circulation and sensation, visual impairment, lower-extremity strength, physical activity, and body mass index (BMI).[13]

Although many of above gait deviations and influencing factors play a major role in diabetic patients to have gait abnormalities,[14] peripheral neuropathy might affect any or all of the above mentioned factors thus playing a major role in gait which is not yet clearly understood.[15] Thus there is a need to explore the role of peripheral neuropathy in gait of diabetic individuals and the objective of this study was based upon this need to evaluate the abnormalities of gait in diabetic peripheral neuropathy (DPN) by reviewing the published studies on assessment and treatment.

Methodology

A systematic review using the following search terms was done and entered into PubMed-(diabetes [Title] OR diabetic [Title]) AND (neuropathy [Title] OR neuropathic [Title]) AND (gait [Title] OR walking [Title]) with search filters activated for articles with abstracts and published in English language. The search was performed by two testers independently and mutual consensus method was adopted periodically. Two main themes were selected under assessment and treatment of gait.

Results

A total of 39 studies (2 excluded-1 abstract not available; 1 not on walking) were obtained in our initial search and after excluding inappropriate articles, a final list of 37 studies were included for data extraction and synthesis.

Assessment of gait in DPN

Gait parameters

Roman de Mettelinge *et al*[16] investigated the effect of peripheral neuropathy and cognition on gait performance in 101 older adults (56 diabetics, of which 28 with peripheral neuropathy and 28 without peripheral neuropathy; 45 matched controls). The study found that older adults with diabetes walked slower, took shorter strides during all walking conditions, and showed more gait variability especially during dual task conditions. Also older adults with diabetes showed that participants with impaired cognitive function walked slower, took shorter strides, and had shorter double support time and increased gait variability when compared to participants with intact cognitive function.

Lalli *et al* measured gait parameters in DM patients with and without diabetic peripheral neuropathy (DPN) during flat surface walking using a portable device (GaitMeterTM). DPN-P participants had greater variability of step length and step velocity, except for DM only participants.[17]

Gomes *et al* assessed kinematic and electromyographic data in 46 subjects (healthy and DN) who walked at two cadences (self-selected and 25% higher) and compared them with different phases of gait cycle. DN subjects showed a delayed peak in plantarflexor activity along the whole cycle (irrespective of cadence) compared with healthy subjects. However, during the imposed cadence, DN individuals showed reduced ankle range of motion along the entire cycle compared with the self-selected condition and healthy individuals walking at

both cadences.[18]

Paul *et al* compared temporal and spatial gait parameters of 15 older people with diabetes and no peripheral neuropathy (DM) and 15 people with diabetes and diabetic peripheral neuropathy (DPN) to investigate the effect of a secondary motor or cognitive task on their gait. Subjects underwent four walks: under normal walking conditions (single task); four times while simultaneously undertaking an additional motor task, carrying a tray with cups of water (dual task); and four times whilst undertaking a cognitive dual task, counting backwards in sevens. Subjects with DPN walked more slowly and with smaller steps compared with those with DM. In general, the secondary task had a significant and adverse effect on the gait parameters and this effect was greater for those with DPN in both absolute and relative terms.[19]

Katoulis *et al* investigated the effect of peripheral neuropathy on gait in diabetic patients by performing gait analysis in 20 normal healthy control subjects (NC), 20 non-neuropathic diabetic control subjects (DC), 20 neuropathic diabetic subjects (DN), and 20 neuropathic diabetic subjects with a history of foot ulceration (DNU). Walking speed was significantly slower in the DNU group compared with the two control groups. The maximum knee joint angle was smaller in the sagittal plane for the DNU group compared with the DC group values. The maximum value of the vertical component of ground reaction force (GRF) was found to be higher in the two control groups compared with the DNU group. The maximum value of the anteroposterior forces was also found to be higher in the DC group compared with the DNU group. The maximum frontal plane ankle joint moment was also higher in the DN compared with the NC group.[20]

Mueller *et al* compared (1) the gait characteristics, (2) the plantar-flexor peak torques, and (3) the ankle range of motion of 10 subjects with diabetes mellitus (DM) and peripheral neuropathy with those of 10 age-matched controls (NODM). The DM group subjects showed less ankle mobility, ankle moment, ankle power, velocity, and stride length during walking than the NODM group subjects. A significant decrease in ankle strength and mobility appeared to be the primary factor contributing to the altered walking patterns of the DM group.[21]

Plantar pressures during gait

Sacco *et al* investigated the ankle range of motion during neuropathic gait and its influence on plantar pressure distribution in two phases during stance: at heel-strike and at push-off in 15 DPN patients and 16 healthy adults and found that DPN patients walked using a smaller ankle range of motion in stance phase and smaller ankle flexion at heel-strike. Peak pressure and pressure-time integral values were higher in the diabetic group in the midfoot at push-off phase when compared to heel-strike phase.[22]

Bacarin *et al* investigated plantar pressure variables during gait and compared 20 healthy controls; 17 diabetic neuropathy patients without foot ulcers; and 10 diabetic neuropathy patients with at least one healed foot ulcer within the last year. The study findings showed that a previous history of foot ulcers in DPN subjects influenced plantar pressure distribution, resulting in an increased load under the midfoot and rearfoot and an increase in the variability of plantar pressure during barefoot gait.[23]

Maluf *et al* assessed the relationship between foot pressures measured during level walking and other types of ambulatory activity in 16 subjects with diabetes mellitus (DM) and peripheral neuropathy (PN), and found that peak pressure and PTI during level walking correlated highly with pressures during ramp climbing and turning at all regions examined and with pressures during stair climbing at 1st and 3rd metatarsals. Correlations between pressures during level walking and stair climbing were moderate at the great toe and poor at the heel. With few exceptions, pressures during ramp climbing, stair climbing, and turning were less than or equal

to pressures during level walking.[24]

Patil *et al* introduced new on-line foot pressure parameters, i.e. normalized peak pressure (NPP) and pressure contact ratio (PCR), which include effects of the weight of the subject, velocity of walking and duration of high pressures in any region of the foot, which were calculated on-line (using specially developed software) would help the clinician to quickly determine the heavily loaded foot areas that are potential sites of ulceration in insensitive feet and take the necessary action to prevent further damage to the foot sole.[25]

Muscle activity-kinetics

Akashi *et al* evaluated the EMG of the right vastus lateralis, lateral gastrocnemius and tibialis anterior were studied during the stance phase, and compared them between three groups: a control group (n=16), diabetic neuropathic group (n=19) and diabetic neuropathic group with previous history of plantar ulceration (n=10). The ulcerated group presented a delayed in the time of the lateral gastrocnemius and vastus lateralis peak occurrence in comparison to control's. The vastus lateralis and lateral gastrocnemius delay demonstrated that ulcerated diabetic neuropathic patients have a motor deficit that could compromise their ability to walk, which was partially confirmed by changes on ground reaction forces during the push-off phase.[26]

Kwon *et al* compared muscle activity and joint moments in the lower extremities during walking between subjects with diabetic neuropathy (DN) and control subjects. The study findings demonstrated that subjects with DN had less ankle mobility, slower walking speeds, longer stance phases, and lower peak ankle dorsiflexion, ankle plantar flexion, and knee extension moments than control subjects. Onset times with respect to heel-strike (HS) for the soleus, medial gastrocnemius, and medial hamstring muscles were significantly earlier during the gait cycle (GC) in subjects with DN than in control subjects. The cessation times of soleus, tibialis anterior, vastus medialis, and medial hamstring muscles were significantly prolonged in subjects with DN. Subjects with DN showed more co-contractions of agonist and antagonist muscles at the ankle and knee joints during stance phase compared with control subjects.[27]

Sacco and Amadio evaluated EMG variables during stance phase in self-cadence treadmill walking under biomechanical and somatosensorial considerations in 20 DPN and 20 healthy controls, and found that the somatosensorial responses and pain tolerance threshold in the diabetic neuropathic group were significantly higher and considered far from the normal patterns. The EMG responses of the thigh and leg muscles in the diabetic neuropathic group were delayed if compared to the normal recruitment pattern, especially the tibialis anterior and vastus lateralis.[28]

Plantar loading responses

Giacomozzi *et al* evaluated 21 healthy volunteers (C) and 61 diabetic patients (27 diabetic subjects without neuropathy (D), 19 with neuropathy (DN), and 15 with previous neuropathic ulcer (DPU)) and found that loading time was significantly longer in neuropathic patients than in control subjects. COP excursion along the medio-lateral axis of the foot clearly decreased from C to DPU groups as well as COP excursion along the longitudinal axis for the DPU group only. The decreased medio-lateral and longitudinal COP excursions and corresponding changes of loading times and patterns supported our hypothesis that a change in the walking strategy of diabetic patients with peripheral neuropathy does occur.[29]

Cavanagh *et al* measured the variability of plantar loading during gait and explored the differences between neuropathic and non-neuropathic patients by studying 39 patients (13 non-diabetics, 13 diabetic non-neuropathic, 13 diabetic neuropathic). The study showed that variability was not significantly influenced by the diagnostic group for any shoe condition or for any region of the foot which suggested

that reduced variability in plantar loading is not a factor in the development of plantar lesions in neuropathic patients.[30]

Methods of gait analysis

Meier *et al* investigated goal-oriented gait termination in 15 healthy elderly and 15 elderly type-2 diabetic subjects and found that the diabetic subjects approached the stopping line more slowly than the healthy elderly subjects. They also exhibited a weaker maximal braking force and a prolonged relative time to develop this force. Despite this slower motion, the centre of pressure overshoots were larger in the diabetic subjects than in the healthy elderly.[31]

Gait-related injuries

Cavanagh *et al* studied two groups of patients from the Pittsburgh Epidemiology of Diabetes Complications Study, matched for age and duration of Type 1 diabetes, but with significantly different vibratory sensation thresholds as determined by Vibratron II testing, and found that the neuropathic group had adjusted odds ratios for reported injuries during gait of 15.0 relative to the control group. The neuropathic group also reported significantly lower scores than the control group on perceived safety in unusual conditions.[32]

Relationship of gait parameters with other factors

Lower limb sensorimotor function and gait

Allet *et al* identified whether frontal plane lower limb sensorimotor functions predicted gait speed and efficiency (step-width-to-step-length ratio) on an uneven surface, in 33 subjects; 21 with diabetic distal symmetric peripheral neuropathy. Hip adduction RTD and ankle inversion RTD predicted 54% of gait speed, with the former predicting the majority (44%). Ankle inversion RTD was the only significant predictor of gait efficiency, which accounted for 46% of its variability.[33]

Menz *et al* evaluated acceleration patterns of the head and pelvis when walking to determine the effect of lower-limb sensory loss on walking stability in 30 older people with diabetic peripheral neuropathy (DPN) and in 30 age-matched controls. Participants with DPN had reduced walking speed, cadence, and step length, and less rhythmic acceleration patterns at the head and pelvis compared with controls. These differences were particularly evident when participants walked on the irregular surface.[34]

Dingwell *et al* quantified the sensitivity of the locomotor system to local perturbations that are manifested as natural gait kinematic variability in 14 patients with severe peripheral neuropathy and 12 matched non-diabetic controls, and found that neuropathic patients exhibited slower walking speeds and better local dynamic stability of upper body movements in the horizontal plane than did control subjects. The differences in local dynamic stability were significantly predicted by differences in walking speed, but not by differences in sensory status.[35]

Walker *et al* evaluated the ability of 30 diabetic and 20 non-diabetic individuals to learn to use a lower extremity sensory substitution device to cue gait pattern changes when they walked on a treadmill at three speeds (1, 2, and 2.5 mph) with auditory sensory feedback to cue ground contact greater than 80% duration of baseline, and found that persons in both groups were able to rapidly and significantly alter their gait patterns in response to signals from the sensory substitution device, by changing their gait cycles.[36]

Courtemanche *et al* examined whether a reduced peripheral sensibility caused by diabetic neuropathy increases the attentional demands necessary for controlling and regulating gait by comparing twelve diabetic patients with peripheral neuropathy and 7 control subjects who performed the walking task, auditory stimuli were randomly presented in the third, fourth, or fifth walking cycle on left foot toe off on left foot heel contact.

DPN patients had a smaller cycle amplitude, cycle speed, and percentage of time spent in the single support phase than control subjects. Also, reaction times while walking were higher for diabetic neuropathic patients than for control subjects.[37]

Brain volume and gait

Manor *et al* measured the relationship between walking outcomes (i.e., speed, stride duration vability, and double support time) and regional gray matter volumes in 29 older adults with DPN and compared it with 68 nonneuropathic diabetic patients and 89 nondiabetic control subjects. The authors found that DPN subjects walked more slowly with greater stride duration variability and longer double support as compared with DM and control subjects. DPN subjects with lower gray matter volume globally and regionally (i.e., cerebellum, right-hemisphere dorsolateral prefrontal cortex, basal ganglia) walked more slowly with greater stride duration variability and/or longer double support.[38]

Muscle activity and gait

Sawacha *et al* evaluated the role of altered muscle activity in gait alterations of 20 diabetic subjects with and 20 without neuropathy, and 10 healthy controls. At initial contact and loading response, an early activation of rectus femoris activity occurred in diabetic subjects with and without neuropathy. During midstance a delay of gastrocnemius activity was observed in diabetic non-neuropathic subjects. During terminal swing a delay of rectus femoris and gluteus medius activity was seen in diabetic non-neuropathic subjects'.[38]

Other comorbidities/complications and gait

van Sloten *et al* evaluated the associations of diabetic complications and underlying pathology with daily walking activity in 100 type 2 diabetic patients without manifesting mobility limitations. Neuropathy was associated with a reduction of 1967 steps/day, decreased muscle strength with 1782 steps/day, and an increase in BMI of 1 kg/m(2) with a decrease of 210 steps/day.[40]

Sacco *et al* investigated the influence of diabetic neuropathy and plantar ulcers on plantar sensitivity, symptoms, and plantar pressure distribution during gait with everyday shoes by comparing three groups: a control group (CG; n=15), diabetic patients with a history of neuropathic ulceration (DUG; n=8), and diabetic patients without a history of ulceration (DG; n=10). Diabetic neuropathic patients presented greater pressure-time integrals and relative loads over a larger midfoot area. Diabetic patients with ulceration presented an altered dynamic plantar pressure pattern characterized by overload even when wearing daily shoes.[41]

Kanade *et al* compared walking capacity between 23 subjects with diabetic neuropathy (DMPN), 23 patients with current diabetic foot ulcers, 16 patients with partial foot amputations and 22 patients with trans-tibial amputations. Total heart beat index (THBI) increased and gait velocity and daily stride count fell with progression of foot complications. The maximum peak pressures over the affected foot of patients with diabetic foot ulcers and partial foot amputations were higher than in the group with DMPN.[42]

Rao *et al* examined the relationship between ankle dorsiflexion (DF) range of motion (ROM) and stiffness measured at rest (passively) and plantar loading during gait in individuals with and without diabetes mellitus (DM) and sensory neuropathy, and found that subjects with DM have reduced passive ankle DF ROM and increased stiffness compared to non-diabetic control subjects, however, subjects with DM demonstrated ankle motion, stiffness and plantar pressures, similar to control subjects, while walking at the identical speed, 0.89 m/s (2 mph).[43]

Electrophysiological findings and gait

Yavuzer *et al* investigated the associations between electrophysiological findings and gait characteristics, in forty-six patients with DM (20 subjects with neuropathy, 26 subjects

without neuropathy) and 20 healthy control subjects. NDPN, but not DPN, group revealed slower gait, shorter steps, limited knee and ankle mobility, lower ankle plantar flexor moment and power than C group, and the difference was statistically significant.[44]

Sacco and Amadio studied the sensitive cronaxie in neuropathic and non-neuropathic diabetic patients as a measure of sensorial deficit and found that the pathological response of the sensitive cronaxie worsened progressively for neuropathic and diabetic patients, respectively. Longer double and single stance times, lower minimum vertical force and lower growth rates were seen in the neuropathic patients when compared to diabetic and non-diabetic subjects.[45]

Foot structure and gait

Mueller *et al* compared foot structure were taken from three-dimensional images constructed from spiral X-ray computed tomography and walking peak plantar pressures between twenty people with DM and PN and 20 people without DM. The study found that combinations of structural and walking variables accounted for 47-71% of the variance in the DM group and 52-83% of the variance of PPP during walking in the control group.[46]

Treatment of gait in DPN

Physiotherapy

Sartor *et al* designed a blinded randomised, controlled trial and studied the effect of a physiotherapy intervention on foot rollover during gait, range of motion, muscle strength and function of the foot and ankle, and balance confidence. The intervention was carried out for 12 weeks, twice a week, for 40-60 min each session as described in their study protocol.[47]

Kruse *et al* administered walking exercise as an intervention in combination with lower-extremity strengthening and balance exercises and studied its effects on balance, lower-extremity strength (force-generating capacity), and fall incidence in 79 DPN patients and found improvements in unipedal stance time 12-month post-treatment.[48]

Shoewear

Sacco *et al* investigated the effect of the participants own shoes on gait biomechanics in 24 diabetic neuropathic individuals compared to barefoot gait patterns and 21 non-diabetic healthy controls. The authors found that walking with shoes promoted an increase in the first peak vertical force and the peak horizontal propulsive force. They also demonstrated a higher peak horizontal braking force walking with shoes compared to barefoot. Diabetic participants also had a smaller second peak vertical force in shod gait and a delay in the vastus lateralis EMG activity in barefoot gait compared to controls. Walking with shoes did not attenuate vertical forces in either group.[49]

Insoles

Guldemond *et al* evaluated the effects of 12 different insole configurations on plantar pressures and on walking convenience in 20 patients with diabetic neuropathy.[50]

The configurations included different combinations of a metatarsal dome, varus and valgus wedges and arch supports with different heights were added on a fitted basic insole. For the central and medial regions, plantar pressure reductions (up to 36% and 39%, respectively) were found when using a dome, standard and extra supports. The largest reductions were achieved with combination of a dome and extra support. The basic insole and a standard support received the best ratings for walking convenience and gradually worsened by adding extra support, a varus wedge and a dome.

Visual feedback

York *et al* examined the role of visual feedback in the reduction of plantar pressures through teaching a "new" gait pattern to 29 olde-aged diabetic peripheral neuropathy

subjects. Subjects were randomized into feedback and no-feedback groups. Instruction to pull the leg forward from the hip to initiate swing rather than push off the ground with the foot while walking was given to all subjects. The feedback group received visual feedback regarding peak plantar pressures after each practice trial. The no-feedback group received no feedback. Peak plantar pressures were significantly reduced from baseline to retention 2 testing at the first metatarsal area in the feedback group. The feedback group walked slower at retention 1 and 1-week testing compared with baseline.[51]

Discussion

The study was aimed to evaluate the abnormalities of gait in diabetic peripheral neuropathy by reviewing studies on assessment and treatment, and there were more number of studies on assessment compared to that of treatment of gait in people with DPN.

Many assessment studies on gait in people with DPN had demonstrated altered gait parameters such as reduced gait speed, reduced double support time, reduced step length, reduced ankle range of motion, with increased ankle invertor-evertor moment; altered plantar pressures with increased load under midfoot compared to rearfoot; earlier muscle activity of soleus, tibialis anterior, vastus medialis and medial hamstrings with delayed muscle activity of vastus lateralis and lateral gastrocnemius; longer loading time with decreased mediolateral and longitudinal center of pressure excursions; with more likelihood for gait-related injuries. The gait deviations were correlated to brain volume, electrophysiological findings, lower limb sensorimotor function, foot structure, muscle activity, and other comorbidities and/or complications of diabetes such as ulcers and foot deformities.

There is a need to study inter-relationships between gait deviations and clinical examination findings,[52] clinical assessment scale scores,[53] neurodynamic examination findings[54] and/or quality of life[55] in people with DPN. The alterations in gait reported in the reviewed studies were much different from either diabetic individuals[56] or neuropathy[57] individuals considered alone thus reflecting the multifaceted multidimensional impact of peripheral neuropathy on gait in DPN population.

Gait-related interventions in DPN population were physiotherapy including walking prescription, lower extremity strengthening and balance exercises, footwear and insoles, and visual feedback which were shown to improve balance, gait speed, muscle activity and plantar pressures in this population. The evidence for intervention of gait and its deviations in people with DPN was limited and there is need for future high quality trials in this population-specific gait changes to medical,[58] surgical,[59] physiotherapeutic,[60] and neurodynamic[61] and/or acupuncture[62] treatment methods.

Future evidence-informed guidelines for DPN should thus incorporate assessment and treatment of gait from a multidisciplinary biopsychosocial perspective.[63]

Conclusion

Many assessment studies on gait in people with DPN had demonstrated altered gait parameters such as reduced gait speed, reduced double support time, reduced step length, reduced ankle range of motion, with increased ankle invertor-evertor moment; altered plantar pressures with increased load under midfoot compared to rearfoot; earlier muscle activity of soleus, tibialis anterior, vastus medialis and medial hamstrings with delayed muscle activity of vastus lateralis and lateral gastrocnemius; longer loading time with decreased mediolateral and longitudinal center of pressure excursions; with more likelihood for gait-related injuries. The gait deviations were correlated to brain volume, electrophysiological findings, lower limb sensorimotor function, foot structure, muscle activity, and other comorbidities and/or

complications of diabetes such as ulcers and foot deformities.

Gait-related interventions in DPN population studied were physiotherapy including walking prescription, lower extremity strengthening and balance exercises, footwear and insoles, and visual feedback which were shown to improve balance, gait speed, muscle activity and plantar pressures in this population.

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