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Diabetic Foot and Exercise Therapy: Step by Step

The Role of Rigid Posture and Biomechanics Treatment

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Abstract: Lower extremity ulcers represent a serious and costly complication of diabetes mellitus. Many factors contribute to the development of diabetic foot. Peripheral neuropathy and peripheral vascular disease are the main causes of foot ulceration and contribute in turn to the growth of additional risk factors such as limited joint mobility, muscular alterations and foot deformities. Moreover, a deficit of balance, posture and biomechanics can be present, in particular in patients at high risk for ulceration. The result of this process may be the development of a vicious cycle which leads to abnormal distribution of the foot's plantar pressures in static and dynamic postural conditions.

This review shows that some of these risk factors significantly improve after a few weeks of exercise therapy (ET) intervention. Accordingly it has been suggested that ET can be an important weapon in the prevention of foot ulcer.

The aim of ET can relate to one or more alterations typically found in diabetic patients, although greater attention should be paid to the evaluation and possible correction of body balance, rigid posture and biomechanics. Some of the most important limitations of ET are difficult access to therapy, patient compliance and the transitoriness of the results if the training stops. Many proposals have been made to overcome such limitations. In particular, it is important that specialized centers offer the opportunity to participate in ET and during the treatment the team should work to change the patient's lifestyle by improving the execution of appropriate daily physical activity.

Keywords: Adapted physical activity, balance, diabetic foot, exercise therapy, gait, limited joint mobility, muscle strength, posture.

INTRODUCTION

Diabetic foot is one of the most ominous complications of diabetes [1]. It is defined as infection, ulceration and/or disruption of deep tissues associated with neurological abnormalities and various levels of peripheral vascular disease (PAD) in the lower limb [2].

Foot plantar ulcers occur in approximately 15% of all diabetes mellitus patients and in 75-85% of cases precede amputation [3, 4, 5, 6].

Neuropathy, vasculopathy, trauma and foot deformities are individually or altogether, the main etiological factors of diabetic foot ulcers [2, 7, 8, 9]. However, in most cases diabetic peripheral neuropathy (DPN) plays a central role [1, 2, 6].

Other factors may contribute to the genesis of diabetic foot ulcer, including limited joint mobility (LJM) [10, 11], muscle weakness [12, 13], poor balance [14, 15, 16], posture and gait alterations [14, 17] which may alone or together, induce abnormal distribution of foot plantar pressure (PP). In diabetic neuropathic patients repetitive pressure under the plantar foot can turn a normal foot into one at high risk of ulceration [1, 18]. One or more of these risk factors are present in more than half of older patients with type 2 diabetes mellitus [1].

There is an important evidence of the effectiveness of regular physical activity as primary and secondary prevention of diabetes and diabetic foot [19, 20, 21]. Physical activity that can be carried out as structured exercise, defined as exercise therapy (ET) or adapted physical activity [21, 22], is aimed to prevent the development or the progression of risk factors for foot ulcer. This review is aimed to consider how ET is able to prevent foot ulcer in diabetic patients.

PERIPHERAL NEUROPATHY

Up to 50% of diabetic patients with type 2 diabetes mellitus suffer from neuropathy that is one of the most important risk factors for the development of diabetic foot ulcers [7, 23, 24].

Diabetic neuropathy has a subclinical onset, is more peripheral than central, is slow to progress, and is mainly sensorial before being motor and autonomic [23, 25, 26, 27]. Lower legs and feet are particularly affected by neuropathy and DPN is the main cause of disability leading to risk of pain, ulceration, and amputation [23, 27].

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The most common type of DPN is distal symmetric polyneuropathy involving the degeneration of peripheral nerves combined with impaired nerve regeneration and reinnervation [27, 28, 29, 30, 31].

Both small and large nerve fibers are involved in a deficit of tactile, vibration, pain and proprioceptive sensitivity [23, 32].

The sensory loss progresses proximally after beginning in the foot [12, 13], and is also associated with a risk of foot trauma or minor injuries due to the lack of protective sensation [2, 24].

Therapy of DNP is difficult because diabetic neuropathies are heterogeneous and affect different parts of the nervous system [23, 33].

DPN is associated with many other anatomical and physiological alterations such as: reduction of motor nerve conduction velocity [34, 35], muscular atrophy, weakness [26, 36], and impaired neuromuscular coordination [37, 38, 39, 40].

In addition, DPN can lead to a reduced sense of limb position [37, 38], less appropriate postural compensatory strategy [39] with prolonged foot reaction time [40, 41, 42], and impaired reflex modulation [47].

All of this contributes to the development of static and dynamic postural instability [48, 49, 50], altered biomechanics and foot loading, with an increase of foot plantar pressure (PP) in the areas at higher risk for ulcer [6, 9, 51, 52].

As a consequence, diabetic neuropathic patients with and without history of ulceration may develop stiff "rigid" feet which are at the same time the cause and the result of the ulcers [53, 54].

These patients have low safety perception and are at a high risk of falling [17, 44, 45, 55].

DPN must be diagnosed at the early stage of the disease but it is difficult because nerve conduction velocity measures do not change early; consequently the sensitivity and negative predictive values of neurological examination are low, also in children and adolescents [56, 57, 58, 59].

Accordingly, it has been well reported that more different functional abnormalities relative to muscular parameters [13, 60, 61], joint mobility [10, 11], balance [62], gait, posture [63], and foot PP distribution [64, 65] are significant for predicting the risk of ulceration before neuropathy becomes clinically detectable.

Thus, evaluation of these functional deficits could be used as screening for: the early detection of patients at high risk of diabetic foot, the appropriateness of ET, and monitoring the patient's condition [60, 66, 67, 68, 69, 70].

The Role of ET

In diabetic patients a regular physical activity reduces body weight, improves blood glucose control and insulin sensitivity [52, 67, 68, 69, 70], which altogether lead to a reduced risk of developing neuropathy [19, 31, 75, 76].

Exercise positively influences other pathological factors associated with DPN, by promoting microvascular function and fat oxidation, by reducing oxidative stress and increasing neurotrophic factors [77, 78].

The effect of ET on glycemic control and variability in patients with type 1 diabetes mellitus, particularly if they had previously a sedentary lifestyle, has not been well demonstrated [79, 80].

Aerobic and resistance exercise training have been the activities traditionally prescribed for diabetes prevention and management [71, 81].

In a 4-year prospective randomized trial, four treadmill sessions per week performed at mild intensity, resulted in a lower risk of developing motor or sensory neuropathy [19].

In another study, one year of diet and exercise counseling in patients with DPN and impaired glucose tolerance significantly improved patients' weight, blood glucose control, cholesterol plasma levels, small nerve fiber functions as well as cutaneous reinnervation [76].

Another study reported improved peripheral nerve function with a reduction in pain and neuropathic symptoms in patients with DPN after 10 weeks of supervised, moderately intense aerobic and resistance exercise [78].

At the same time the presence of a neuronal impairment threshold beyond which it is difficult to reverse the negative effects of disease by ET, has been suggested [76, 82].

PERIPHERAL ARTERIAL DISEASE

Diabetes is one of the most prominent risk factors for peripheral arterial disease that is a component of systemic atherosclerosis [83, 84].

Hyperglycemia and hyperinsulinemia have a role in the endothelial damage, abnormal vascular functioning and lead to an higher atherogenesis susceptibility. Therefore diabetic patients may develop atherosclerosis and the related PAD more easily than non-diabetics [74, 77, 84].

Changes in the large vessels and microcirculation associated to endothelial dysfunction and inflammation may cause ischemia and, then, fibrosis of connective tissue in the diabetic foot [85, 86, 87].

All of these has an important role in the development of foot ulcers, affecting also negatively the subsequent healing [2, 4, 18, 61].

Functional limitation in PAD such as intermittent claudication has been traditionally attributed to the decreased blood flow induced by arterial obstruction and an impaired endothelial vasodilator [88, 89].

These patients may have a deficit of foot muscle energy reserves, mitochondrial dysfunction and consequently a greater susceptibility to fatigue [89, 90, 91, 92].

Peripheral vascular disease and neuropathy are frequently present in the same patient, consequently, 50–58% of all diabetic foot ulcers are ischemic or neuroischemic [93, 94].

Diabetic patients with peripheral arterial disease (PAD) can have rest pain, claudication, and lower walking speed, which reduces their walking distance and their daily physical activity [83, 95].

Neuropathy can reduce leg symptoms and explains the absence of rest pain or claudication [1].

The prevention and the treatment of these functional problems are important because the diabetic patient's sense of self-efficacy and independent lifestyle are significantly associated with his/her ability to walk [95, 96].

The Role of ET

Exercise training increases functional capacity, reduces fatigue, exercise pain tolerance and decreases claudication [83, 91, 97, 98].

The positive effects of ET are connected with an improvement in endothelial function, oxidative stress, markers of adiposity and, inflammatory responses. Moreover physical activity improves perfusion and plasma viscosity facilitating oxygen delivery, skeletal muscle metabolism and strength in diabetic patients with PAD [19, 74, 77 83, 99].

Patients with claudication pain who do intermittent walking for more than 30 minutes, three times a week, signifycantly improve their capacity to walk distances [98, 100].

Type 2 diabetic patients with PAD, after a 6-month home-based walking program, have improved walking speed and quality of life [95].

Walking therapy and a supervised exercise are, therefore, an essential element in the management of these patients [89, 95, 101, 102].

MUSCULAR DYSFUNCTION

Diabetes is associated with lower extremity muscle problems that are an important risk factor for ulcer [36, 103].

In both type 1 and type 2 older diabetic patients there is a faster decline of muscular mass and muscular strength compared with age-matched healthy controls [36, 104, 105].

Muscle atrophy is connected to axonal loss followed by incomplete re-innervation [29, 30, 76].

Although muscle atrophy and weakness are linked to the presence and severity of neuropathy [13, 26, 60], it has been reported that foot muscle atrophy and muscle activity alterations may occur before detecting peripheral neuropathy by standard clinical techniques [39, 60, 103].

Muscle alterations start in the feet and then progress proximally, especially with leg involvement [13]. Even the proximal part of the lower limbs and trunk may be affected by muscle atrophy [104]. As a result, the total volume of foot muscle is halved with a decrease of muscular units and quality (strength per unit of muscle mass) [75, 106, 107, 108] in the thighs, legs and feet in long-term DPN patients [12, 36, 107, 109, 110].

In the muscles of type 2 diabetes mellitus patients the type of fiber distribution is correlated with the severity of insulin resistance and there is a minor percentage of slow oxidative type I fibers and lower oxidative activity [111, 112]. Foot muscle energy reserves can be reduced, even in early stages of the disease, before the development of clinical neuropathy [61, 88].

Alterations in muscle activity occur during quiet standing or walking [39, 113]. It has been reported that diabetic patients, irrespective of DPN [63], have significantly different lower leg muscle activation compared to healthy control subjects when walking [39]. DPN patients also have more co-contractions of agonist and antagonist muscles at ankle and knee joints when walking [37, 38, 40]. Consequently, the rectus femoris, soleus, medial gasrocnemius, and medial hamstring muscles are activated early while the average cessation time of the rectus femoris, soleus, tibialis anterior, vastus medialis and medial hamstring muscles is significantly delayed [39, 40]. This altered muscle activity can be connected to the adoption of a safer and more stable gait pattern [40]. In particular, DPN may cause less capacity to brake the forward momentum of the body just after heel-strike, leading to a prolonged increase of forefoot PP [40, 114].

For many years foot muscle atrophy and muscle imbalance have been suggested to play an important role in the genesis of foot deformities [36, 115, 116, 117]. In particular it has been hypothesized that the loss of foot muscles precedes the development of toe abnormalities and metatarsal prominence, thus increasing the risk for ulcer [36].

Finally, it has been well-documented that muscle weakness can induce physical disability [106, 118], and is associated with less daily walking activity, balance deficit, slow gait, walking instability, and a higher risk of falling [17, 118, 119, 120].

The Role of ET

Diabetes and aging reduce the force-generating capacity (strength) of skeletal muscles, but this can be increased by physical exercise at all ages [45, 121, 122, 123, 124]. It has been suggested that an ET program can overcome this vicious cycle in diabetic patients and significantly improve their muscle strength [22, 82, 125].

It has been reported that an unsupervised exercise program improves joint mobility [126], walking performance [82, 119], postural stability [45], muscle quality [75], and increases lipid storage in muscle as well as fat oxidation capacity [96].

In patients with DPN the muscles at ankle level may be reduced by 40%-60% [12, 108, 127, 128], but may be temporarily recovered by a few weeks of ET [82, 125, 129].

Another study shows that lower extremity and trunk strength increase by 31.4% after 6 months of resistive training [130], while 12 weeks of ET are sufficient to significantly improve hip, knee and ankle muscles strength even in the presence of sensory neuropathy [22, 82, 125, 129].

In type 2 diabetic patients 16 weeks of strength training increase lower body strength, improve glycemic control, muscle quality, and muscle fiber hypertrophy. This has increased in parallel adiponectin levels and decreased free fatty acid and c-reactive protein levels [75].

Ultrasonographic images suggest that the ratio of connective tissue to streak muscular tissue can be modified by ET inducing muscular hypertrophy. Thus, it is evident that the decline in musculoskeletal fitness in diabetic patients often

resulting in disability, may in fact be reversible [127, 129, 130].

The direct effect of muscle strength improvement on foot PP distribution and the prevention of foot ulcer is unclear [131]. In the same way it is not known whether improved muscle strength is combined with improved muscle quality and coordination.

JOINT MOBILITY

Plantar Fascia and Achilles Tendon

Diabetes is associated with overall thickening and stiffness of the main tendons and ligaments of the foot-ankle complex, *i.e.* the plantar fascia (PF) and Achilles tendon (AT) [132, 133, 134, 135].

It has been reported that the PF thickness is a measure of tissue glycation and it is longitudinally associated to the development of complications in type 1 diabetes mellitus patients [135, 136].

Besides the glycosylation of collagen, several other pathophysiological mechanisms may be involved in the development of AT and PF thickening such as inflammation, microvascular disease, overuse and trauma [134, 137].

It is well documented that the quality of gait and posture are also connected to the capacity of AT, PF, and metatarsophalangeal joints to work synergistically [54]. The correct functioning of these structures maintain the longitudinal arch of the foot in a correct position, absorb shock during landing, maintain correct foot rollover and perform propulsion efficiently [53, 24, 138].

In diabetic patients overall joint tissue damage can influence joint function, limit the range of motion and induce foot PP alterations in both orthostatic and dynamic conditions [53, 134]. It has been hypothesized that the overall thickening of the foot's structures contributes to keeping the foot in a cavus configuration with subsequent abnormal loading [54]. AT and PF thickening, which is more evident in DPN patients, causes rigid foot [54] and is directly correlated to ground reaction forces under the metatarsal heads [53, 66], resulting in a higher risk for plantar fasciitis and foot ulcers [134]. The increase in tensile force exerted by the AT on the calcaneus reduces foot dorsiflexion, thus worsening PF tension [9, 139, 140]. Accordingly, ankle, subtalar and metatarso-phalangeal joint mobility and biomechanics will be altered [133].

During gait, diabetic patients show attenuated mild changes in AT length [141] associated with limited ankle dorsiflexion and a redacted leg rolling over the foot during the late stance phase [51, 66]. All this is associated with excessive forefoot PP, then recurrent skin breakdown and delayed wound-healing [139, 142]. If the AT is lengthened, ankle dorsiflexion increases, peak PP and the recurrence of neuropathic plantar ulcers on the forefoot are reduced [139, 143, 144]. It is important to note that, despite the presence of AT thickening in DPN patients, the simultaneous kinematics and kinetics indicate excessive dorsiflexion of the midfoot and forefoot during gait which are associated with high PP [145]. These results suggest that, in static and dynamic conditions, despite the action of the AT that involves alteration of the foot's posture in extension, diabetic patients must exert greater force to put the ankle in dorsiflexion, thus increasing even more the foot's stiffness.

Foot biomechanics are also affected by PF alterations. PF plays an important role in sustaining the longitudinal arch of the foot during propulsion [140, 146] PF stiffness may involve a lower first metatarso-phalangeal joint range of motion (ROM) which in turn, in association with toe deformities (hyperextension), increases PF tension, thus leading to a steadily rigid foot and high longitudinal arch [54].

Paradoxically, it has been suggested that a greater proportion of midfoot stability during gait has been linked to modified/stiffer soft tissue such as the plantar fascia in diabetic subjects [147, 148].

Finally, it is unclear if abnormal posture and biomechanics (*i.e.* conservatory strategy) [43, 138] can in turn induce specific overuse of the AT and PF in diabetic patients. Overuse is recognized as the major pathogenetic factor for increased thickness of the AT and plantar fasciitis [134]. At the same time there are few studies on the role of lower leg and foot thickening on general body posture.

Limited Joint Mobility

Limited joint mobility is an important risk factor for neuropathic plantar foot ulceration. It is defined as painless complication of diabetes caused by thickening and stiffness of periarticular connective tissue [10, 11, 149, 150]. Joint mobility decreases with aging [126, 151, 152], but it is more evident in diabetic patients [67, 153, 154], in relation to the duration of diabetes, glycemic control and DPN level [11, 46, 66, 155]. Limited joint mobility is widespread in the diabetic patient's body and has an insidious onset followed by an asymptomatic progressive deterioration [10, 11, 153, 154]. A reduction of normal range of motions in the affected joints can occur just a few years after diagnosis, even in young patients [152, 153, 156].

The etiopathogenesis of limited joint mobility in diabetes has not been fully explained although the main causal factor seems to be the effect of metabolic disorders in the increased stiffness of skin, joint capsule, ligaments and tendons [66, 86, 134]. The main biochemical abnormality in joint tissue of diabetic patients is the excess of non-enzymatic glycosylation of collagen, with a production of advanced glycation and products (AGEs) which in turn lead to an increase in collagen cross-links. The increase of inter- and intramolecular cross-linking of collagen fibers alters the mechanical properties of these tissues with a decrease in elasticity and tensile strength, thereby enhancing mechanical stiffness [134, 157, 158].

At the same time, other diabetic complications such as microangiopathy may cause ischemia and then fibrosis of connective tissue with a negative effect on the joint's ROM [86, 134]. Neuropathy, muscle weakness, and the reduced use of joint ROM, may in turn increase the joint's deficits [46, 126, 134, 159].

Limited joint mobility is correlated to a foot's peak PP, pressure–time integrals and shear forces [10, 11, 66, 150, 160]. A deficit of ankle ROM induces small foot dorsiflexion at landing and contributes in reducing the heel strike phase

and the late stane phase of the gait. As a consequence, foot landing occurs with the most anterior part of the heel [51, 66, 161].

The deficit of the subtalar joint plays an important role in the development of abnormally stiff "rigid" feet that is a cause of greater PP and abnormal gait in diabetic patients. The deficit in joint excursion makes the foot less flexible and less able to dissipate the impact of the ground during the heel-strike phase [156]. Subsequently, the foot limited joint mobility increases the difficulties in inversion/eversion, affects the rolling during mid-stance and does not allow proper preparation of the push-off [62, 66, 147].

Finally, metatarso-phalangeal limited joint mobility and the impairing of forward body weight induce altered foot propulsion and increase the load at the metatarsal heads [150, 161]. Consequently, load is accumulated at the forefoot during the whole stance phase [51, 66].

The effects of diabetic foot on the trunk, coxofemoral and knee ROM are not fully understood yet. It is instead well known as the hamstring tightness may induce prolonged forefoot loading and plantar fasciitis [163, 164, 165].

Considering that limited joint mobility is evident before the development of clinical neuropathy [103, 150], and that it is correlated with other chronic complications of diabetes, it has been suggested that assessment of ankle and foot joint mobility can help define the risk for ulcer and monitor the patient's condition [66, 69, 70, 150, 155, 166, 167]. This is possible today because the trend of ankle and foot joint mobility in aging and diabetes is well known and threshold values relating to ulcer risk have been identified [66, 67, 150, 153]. Joint mobility can be easily and rapidly detected by a goniometer or inclinometer, thus identifying the foot at higher risk in about 80% of cases because ulceration is more frequent on the side of the foot with the least limited joint mobility [10, 66, 67].

The Role of ET

Joint ROM deficit in diabetic patients is due to periarticular limitations (*i.e.*, muscle, tendon, joint capsule, ligament, skin) [134], and improves after a few weeks of therapy [22, 82, 129].

Stretching exercise is often prescribed to help relieve AT-PF tension with an attempt to reduce arch deformation, excessive pronation, rearfoot valgus, and improve ankle dorsiflexion and PF tension [20, 21, 140, 168, 169]. Moreover, less AT stiffness can reduce forefoot PP and improve the quality of stance phase.

In particular, triceps surae and hamstring stretching can even be recommended for the treatment of plantar fasciitis, the shift forward of center of pressure and the prolonged forefoot loading in static and dynamic conditions [145, 153, 165].

In patients with DPN, limited joint mobility, ankle and foot ROM improve significantly after 5 weeks of passive joint mobilization [20].

Ten-twelve weeks of unsupervised home exercise therapy can significantly increase ankle mobility in DPN patients, making the difference not significant compared to the healthy controls subjects [20, 22, 129].

In a randomized controlled study of 19 diabetic patients without history of foot ulceration, the peak PP decreases significantly for each period of the gait cycle after unsupervised home ET of active and passive ROM activities for foot joints [21]. Unfortunately, it is not well understood yet whether improvement of ankle and foot joint mobility, after a period of ET, would be effective in preventing foot ulcer. But it has been suggested that a simple, routine, home exercise program for diabetic patients could result in fewer ulcerations of the plantar foot [21] and also help the patient to be functionally independent [170].

The positive effects exerted by active and passive joint mobilization confirm that the use of the joints for the full range of motion is necessary to maintain good joint mobility [82, 159]. Consequently, there is a need to restore a physiologically positive gait pattern to maintain during daily living activities of diabetic patients taking care not to expose to risks of tissue injures [148].

BALANCE, POSTURE AND GAIT

A complex set of balance, posture and gait alterations can be present in diabetic patients which increases the risk of plantar ulcer [17, 48, 49, 171]. Although these alterations can be present in diabetic patients regardless of whether they are DPN [63], it is well documented that the progression of DPN is correlated to balance and muscle strength deficit [12, 49, 172]. Impairment of postural control and weakness together with limited joint mobility foot deformities leads to posture and gait alterations [40, 150, 173]. This process creates a vicious cycle which results in increased foot PP and risk for ulcer. It is well known that postural control while standing is reduced since early stages of neuropathy and that the balance deficit increases the frequency of injuries and falls [17, 45, 62, 120].

The quality of balance is linked to vestibular, somatosensory, visual sensitivity and motor outputs [174, 175, 176]. Each of these afferent and efferent systems can be compromised in diabetic patients but somatosensory sensitivity and motor outputs are more susceptible to damage by DPN [23, 25, 62]. Diminished somatosensory information and the delay in motor outputs in feet, ankles and legs can result in the lack of feedback, higher reaction time and deficits such as a decrease in rapidly available ankle strength [43, 113, 177].

Static posturography evaluation in quietly standing DPN patients shows a lower body sway control with a trace made by the center of pressure that is significantly larger and longer than in diabetic patients without DPN and healthy controls [113, 178, 179].

DPN patients show a significantly wider distance between center of pressure (COP) and center of mass (COM) in anterior-posterior and medial-lateral positions in comparison to healthy age-matched subjects. This difference is more evident when patients' eyes are closed, and in medial-lateral directions [109] and indicates the presence of higher horizontal acceleration of the COM [176].

Balance problems are more evident in patients with history of falls but even in diabetic subjects without experience of falls there is a deficit of balance similar to that of non-diabetic subjects with a history of falling [120]. Diabetic patients with a history of falls may show an increase of COP velocity and lower COP motion in more challenging tasks (*i.e.* vision) compared to controls without a history of falls [120]. This condition can be a consequence of more proximal somatosensory input and joint use (knee-hip) in the balance control, *i.e.* proximal control, and increased body stiffness can be present [120].

The presence of foot deformities does not appear to significantly affect standing balance although it has been reported that claw or hammer toes may induce greater postural sway [173].

There has been a lot of attention focused on the evaluation and treatment of gait abnormalities in DPN patients because they are important factors in the primary and secondary prevention of foot ulcers [48, 180]. The presence of DPN involves searching for a different safer posture and the necessity to change the walking strategy [43, 181]. DPN may induce a diminished perception of leg or foot position, ankle movement, and the type of foot contact with the ground [41, 42, 43]. As consequence, during gait, these patients may have difficulty understanding when they can safely transfer their body weight from limb to limb [42, 43, 182]. These deficits, together with the presence of a steady rigid foot, lead to a gait similar to flat-footed walking, in which the foot arrives on the ground almost flat due to lower ankle dorsiflexion [51, 161, 181]. The gait is characterized by a minimal heel strike phase due to the difficulty in controlling the legs' deceleration, and in braking the forward momentum of the body [52, 114, 160]. The presence of a steady rigid foot involves lower foot pronation at initial contact and lack of physiological helical movements of the foot during the stance phase [54, 138]. All this during mid-stance is associated with less ankle movement (flexion–extension) and difficulty in the foot's inversion/eversion [40, 51, 63, 147]. This does not allow the physiological passage of the foot from a flexible to a rigid condition, necessary to adequately perform the foot's push-off [181]. Moreover, the stance phase is characterized by abnormal foot rolling and a difficult forward progression of the body weight [51, 66].

In healthy subjects during the heel off stage the COP has a medial shift on the medial metatarsals [183].

This load shift is necessary to perform a correct foot push-off [183]. Instead, in diabetic patients during the stance phase the mid-foot is in excessive dorsiflexion, external rotation, eversion [145] and the foot performs the push-off at the metatarsal level with minimal involvement of the hallux [161].

During gait the COP progression time percentage in the sub-phases is approximately 7.0% initial contact, 4.8% loading responses, 48.8% mid-stance (foot flat phase), 39.4% forefoot push-off phase [183]. This type of stance phase distribution changes in diabetic patients. The presence of rigid feet and the decrease in walking speed, typically present in patients with diabetes, increases the time percentage in mid-stance and in double support while decreasing time in heel contact and forefoot push phases [43, 63, 160, 161, 181]. All of this induces an alteration of rhythmic acceleration patterns during gait [44].

There is also a progressive shift of the step's fulcrum from the tibio-tarsal (ankle strategy) to the coxofemoral joint (hip strategy) involving greater use of the proximal hip's musculature to push the legs forward with less use of the plantar flexor muscles [63, 178, 181, 184].

At the same time DPN patients show more co-contractions of agonist and antagonist muscles at the ankle and knee joints that can be connected to the adoption of a safer and more stable gait pattern [38, 40]. This condition is confirmed by the presence, in diabetic patients with and without neuropathy, of an early rectus femoris activation which could be finalized to stabilize the hip and knee joint during the heel strike, decelerating the forward motion at the hip and knee [39].

It has been reported that in neuropathic patients the hip flexor, extensors and flexors of the ankle and the knee flexors muscles are weak while the knee extensors and the abductor muscles show normal strength compared to healthy subjects [105, 109]. In DPN patients this may be explained by the presence of lower gait speed and by the difficulty in controlling the medium-lateral sway that is particularly high during heel-strike and propulsion [44, 109, 160, 161, 171]. It is well known that the abductor/adductor muscles play a dominant role in the control of medium-lateral sway while the ankle muscles (plantarflexors/dorsiflexors) are dominant in controlling anterior-posterior balance [176]. Using a wider stance and lower COP excursion could be a strategy to compensate for instability in the medium lateral direction while the presence of knee and ankle flexion could compensate for instability in anterior-posterior direction [120, 185].

In addition to ankle and foot problems, diabetic patients' knee, hip, trunk mobility and posture deficit can affect their balance control [14, 39, 181, 186]. It has been reported that DPN patients may show an anteverted position of the pelvis in static and dynamic conditions compared to diabetic patient without DPN and healthy control subjects. These findings are unexpected because there is a high prevalence of pes cavus in DPN patients that is normally associated with backward displacement of the pelvis and a posterior pelvic tilt [63].

It has also been reported that subjects with impaired glucose tolerance and peripheral neuropathy have less trunk control [187], and elderly people with diabetes exhibit forward trunk lean during walking [188]. This may contribute to explain why DPN patients have a "flat-footed" gait. At the same time the flexion of all major lower limb joints in the search for greater postural control could be a further explanation.

As consequence, instead of a rigid foot, it is possible to speak of rigid posture in DPN patients.

It is unclear whether assumption of abnormal postures (rigid posture) in diabetic patients can lead to tightness of the lower limb muscles, thereby inducing negative effects on the foot. More simply, it is seen that, with time, neuropathic patients develop a certain gait characterized by hip strategy [181], lower gait speed [14, 171], wider stance [185], re-

duced gait cycle amplitude [43, 181], reduced ankle-foot mobility, and more carefulness to avoid falling with a more cognitively dependent gait control [43].

The Role of ET

It has been suggested that ET could be highly clinically relevant in improving and maintaining the foot's biomechanics in restoring a physiological pattern. The achievement of these results could decrease peak PP during daily living activities [51], which is the most important factor for prevention of plantar foot ulcer in the case of ET.

It is well known that diabetic patients' balance and trunk proprioception can be improved with just a few weeks of training [45, 82, 189]. Three weeks of daily exercise, designed to increase rapidly available ankle strength, improves balance in older patients with mild to moderate DPN [190]. In older patients with mild-to-moderate DPN, proprioception, foot reaction time and leg strength improve after 6 weeks of balance/strength training. Moreover there is a reduction in the risk of falling and postural sway [45]. Another study showed that balance, gait speed, and the fear of falling improve after 12 weeks of training in older type 2 diabetic patients [82].

A further study showed that patients with a history of falls had lower COP velocity and increased COP regularity after a 6-week training intervention with positive effects on balance and postural control [120]. The daily step count and 6-minute walking distance both improved by weight-bearing treatment more than by no-weight-bearing exercise in another study of DPN patients [191].

It has been reported that some walking patterns can be used to reduce the forefoot peak plantar pressures (shuffling gait, hip pull-off, step-to walking, backward walking) in DPN patients [192, 193, 194].

It may be possible that these adapted walking patterns can cause other adverse musculoskeletal, posture and biomechanical effects on the spine, hip, knee, or ankle joints [192].

For this reason seems more appropriate to maintain or restore a physiological posture and a correct walking.

PLANTAR PRESSURE

The relationship between the area of high PP in orthostatic and dynamic conditions and the site of plantar ulceration has been suggested and studied for many years [180, 195]. It is known that not only does the presence of high foot PP result in ulceration [196] but it is the combination of high PP and foot insensitivity that completes the causal pathway [3]. Therefore, the persistence of high foot PP during standing and repetitive pressure under the foot during walking, together with the lack of peripheral protective sensation, lead to skin thickening and callus formation which, in turn, increase loading even more and can induce subcutaneous hemorrhage and ulcer [1, 18].

It is well known that plantar pressure abnormalities occur early in the natural history of neuropathy and that the sites of peak pressure can change over time [65, 197]. It is also well known that development of high PP in diabetic patients is a result of several factors. A greater prevalence of foot deformities and reduced plantar foot contact area on the ground can be present in neuropathic patients [51, 145, 198, 199]. Foot deformities such as hammer and claw toe, hallux valgus, prominent metatarsal heads, and pes cavus are considered the main causes of the development of high pressure sites leading to the majority of diabetic foot ulcers [6, 199, 200].

Hammer and claw toes involve hyperextension of the metatarsal-phalangeal joint and therefore the progressive toe's unloading is associated with an increase of weight-bearing pressure on the metatarsal heads [51, 117, 160]. Moreover, at the metatarsal heads there may be less subcutaneous tissue and distal displacement of the protective fat pads associated with an increased risk of foot ulcer [9, 201, 202].

For some years, even in the absence of a clear scientific evidence, it has been commonly accepted that the deformities associated with the diabetic neuropathic foot were the result of muscle atrophy and an imbalance between the foot's intrinsic and extrinsic musculature [115, 116].

More recently this theory has been questioned. In fact, although the relationship between DPN and muscle atrophy in the lower limb and foot has been confirmed, the link between atrophy and foot deformity development seems not so closely correlated [35, 202].

One possible explanation of foot deformity development is that, together with a deficit of the foot's muscles, even the overall thickening of the connective tissue has an important role [54, 138]. The effects of balance, posture and gait deficits on the development of connective tissues alterations and foot deformities have not yet been explained. Rigid foot/posture as result of diabetes has an important role in the development of high foot plantar pressures. During the heel strike and loading response there is less ability to absorb shock and transverse rotation [10, 54].

In DPN patients the COP slight medial shift at the heel-strike and the relatively fast initial foot pronation (subtalar eversion) are reduced. Therefore there is less foot flexibility and less capacity to absorb the ground reaction force [52, 54, 147, 161]. These patients have a short heel-strike phase associated with a foot landing with the most anterior part of the heel and with an early loading of mid-foot and forefoot [161].

The subsequent displacements of COP during the stance phase are also altered. The lateral shift of COP, that indicates the load delivering toward the lateral foot's border, the medial shift of COP on the medial metatarsals and the great toe at the heel off stage are progressively reduced in diabetic patients. As a result DPN patients show a significant reduction of COP displacement in both mediolateral and anteroposterior directions during gait, associated with plantar foot overloading compared to non-diabetic subjects [51, 52, 161].

The result of an abnormal COP trajectory is a forward shift of the pressure patterns with a concentration of PP in the metatarsal area [114, 203, 204]. The medial and lateral forefoot sagittal plane excursion during gait is negatively associated with the pressure time integral sustained respectively under the medial and lateral forefoot [52]. In healthy subjects the heel is in contact with the ground for about two-

thirds of the initial stance phase while the forefoot and toes are in contact for about the last 60%. As a consequence the flat-foot interval, in which both the heel and the forefoot are in contact with the floor, occurs approximately during the middle 23% of the stance phase. At the same time the vertical ground reaction force component is characterized by two peaks of foot loading. The first peak is related to the landing response on the heel, and the second peak is related to the pushing off with the forefoot at the end of stance. Walking speed influences the distribution of the percentage time in the different sub-phases during the stance phase and the foot-loading peaks [160, 205, 206].

Diabetic patients walking slowly have a longer double support time, longer stance phase and shorter steps. Therefore the mid-stance phase is prolonged while the "loading response" and the "terminal stance" phases are reduced. Consequently the forces generated at the moment of the heel-strike and push-off decrease (peak PP) while the time when the entire foot remains in contact with the ground increases. All this, together with the reduction of the plantar support surface, involves a higher pressure-time integral even in the rear foot, mid-foot and forefoot.

The effect of different risk factors for ulcer such as: early contact of the forefoot with the ground, the effect of AT and PF thickness, the push phase performed at the level of the metatarsal heads, and the presence of foot deformities [173] exposing the metatarsal-head zone to higher risk ulcer, is well known. However, it has been reported that the forefoot/rare foot plantar pressure ratio is increased only in severe diabetic neuropathy [204].

In addition to the vertical force component, the role of shear stress on the plantar surface during gait has been studied [103, 207]. Local shear stress distribution is correlated to pressure distribution. It has been reported that there is a statistically significant increase in the mediolateral component of ground reaction force at the metatarsal area in diabetic patients with history of neuropathic ulcer compared to healthy control subjects. Instead the mediolateral component is lower in the big toe than in diabetic patients with history of ulcer. It also has been reported that there is a significant decrease in tangential force (anteroposterior component) in the heel and entire foot in patients with a history of neuropathic ulcer compared to healthy volunteers [160].

However, the major difficulty in the definition of the role of shear stress in the development of plantar ulcer is associated with the difficulty in obtaining reliable and meaningful results by using the available measurement systems. New assessment methods have recently been proposed regarding the tangential stress [103, 145].

With regard to the role that daily activity plays, it has been suggested that individuals with diabetes who develop ulcer in the 37.1± 12.3 week follow-up period, may have lower overall daily activity than their non-ulcerated counterparts. Furthermore, individuals with a previous history of ulceration were more active than those who developed an ulcer [208]. At the same time it has been reported that diabetic subjects with a history of recurrent plantar ulcers have significantly less daily activity and stress on the plantar foot than diabetic patients without history of ulcer or healthy subjects [209].

The Role of ET

There is no important research on the positive direct effect of ET treatment on foot PP, but as reported in this review, serious foot PP is the last ring of a long chain and many of the other rings can be treated by ET. A specific physical activity finalized to reduce weight loss and functional deficit related to DPN such as muscular weakness, poor balance, and limited joint mobility, could improve the quality of PP distribution [3, 11, 22, 119, 150]. Treatment of static and dynamic posture alterations may also help correct the redistribution of PP.

An increased weight-bearing activity (moderate walking) seems do not increase the risk of foot ulceration in diabetic patients with DPN or a prior history of foot ulcer [71, 210]

Daily inspection of feet and the use of protective footwear is recommended for the prevention and an early detection of ulcers [2, 71, 211].

In patients with unilateral diabetic foot complications, ET protocols may reduce the load increase on the unaffected limb [211], thereby reducing the risk of plantar injury by avoiding the beginning of new abnormal posture. It has been suggested that alternative forms of partial or non-weight bearing aerobic exercises could be considered supplementary to essential walking exercise for improving the level of physical fitness and glycemic control in patients at high risk of neuropathic ulcer [211]. For many years the usefulness of modifying the walking pattern [181, 192, 193, 212] of neuropathic patients in order to reduce the risk of ulcer induced by high pressure has been suggested. Unfortunately there are no data on the effectiveness of this interesting therapeutic solution in the prevention of ulcers, muscular and skeletal systems.

The risk associated with the use of these therapeutic solutions is to feed vicious postural cycles instead of solving them. Perhaps a more interesting solution would be to correct the static and dynamic posture rather than the gait [51], thus correctly distributing the foot's plantar pressures and respecting the needs of the whole body.

DISCUSSION

This review shows the complexity of alterations in the lower leg and foot in diabetic patients and the ways in which they can affect balance, posture and the biomechanics of the whole body. We also have highlighted the role of ET in the prevention and recovery of these anatomical and physiological deficits.

In diabetic patients DPN, peripheral arterial disease and non-enzymatic glycosylation of collagen are the main contributing factors to the development of limited joint mobility, muscular impairment and foot deformities [36, 46, 117, 135, 150, 154]. As consequence there is a progressive development of poor balance, then posture and biomechanical alterations [63, 178]. These impairments feed a vicious cycle that progressively alters the PP distribution and worsens the condition of the feet.

Over time, in orthostatic and dynamic conditions, the increase in plantar pressures in some areas of the foot associated with a deficit of peripheral protective sensation, leads to a higher risk of skin breakdown and ulcer [11, 150, 204]. Some of the functional deficits correlated to diabetic foot such as limited joint mobility, muscle weakness, poor balance, lower gait speed and less walking are well known and have been treated by ET programs [20, 45, 82, 130]. The recovery of these functional deficits can be done in a few weeks, achieving insignificant differences compared to age-matched healthy controls [20, 22, 129]. These results are very important because such factors as limited joint mobility and muscular abnormalities are considered important risk factors for foot ulceration in diabetic patients with a direct impact on the quality of posture and gait [11, 13]. The problems that patients have with balance mean they are at high risk of falling and conservative postures may lead to abnormal PP [43, 138]. It is important to emphasize that the first studies on the effects of physical activity on the progression of DPN have shown positive results [19, 56, 76, 78]. It is also known that the excess of non-enzymatic glycosylation of collagen is due to reduced metabolic control [134, 156] that improves with the regular practice of proper physical activity.

However, to date, some aspects of the relationship between ET and diabetic foot ulcer prevention remain unclear. It is not clear if other risk factors for ulcer (*i.e.* foot deformities, abnormal foot roll-over) can be treated by ET, if the improvements achieved persist over time, and especially if the results have a real preventive effect on ulcers. It is evident that the correct distribution of foot plantar pressure in quiet standing and during gait is one of the most important results in the prevention of diabetic foot ulcer. The foot's abnormal plantar pressures are not only related to the presence of foot deformities but may also be due to other factors such as altered static/dynamic posture or an altered foot roll-over while walking [145, 160]. The quality of posture and gait is directly related to the quality of somatosensory sensitivity [176], so the treatment of diabetic patients, particularly if affected by neuropathy, should be focused on correction of posture and foot roll-over disorders. Unfortunately, there are very few studies that have investigated the relationship between DPN, abnormal body posture and foot PP alterations [14, 63, 185]. As a consequence, there are no studies that examine the effects of correction of postural and gait alterations on foot plantar pressure and ulcer prevention.

It is difficult for patients to do ET on a long-term basis and if the ET program stops the patient experiences a gradual loss of normal performance [20, 82, 130]. The positive response of diabetic patients to the training and the progressive loss of the improvements achieved after completion of the training period suggest that patients may have difficulty in moving correctly during daily living activities (*i.e.* to stimulate the function). From this point of view, the presence of diabetic neuropathy seems to have a central role. For this reason ET programs should also aim to teach patients the correct movements and postures to use during daily life activities and seems to be a valid strategy in maintaining the results achieved over time.

The possibility of achieving positive effects by ET in the prevention of diabetic ulcers is determined by the involvement of patients and the drop-out rate which can be high. However, one of the goals of ET is to educate and counsel patients [213, 214], so as to increase their involvement in the ET programs, improve the enrolment and adherence of patients as well as reduce the typical high dropout rate of ET therapy, which can be up to 40% [80, 125, 130, 131], as reported in many studies, and promote long-term participation [82, 215, 216].

It is also possible to improve ET program attendance by the use of home-based protocols, diaries and tools for evaluation of daily physical activity [95, 129, 217]. It can also be useful to make telephone calls, schedule periodic meetings with patients and monitor the therapy results, especially during the first phase of treatment [74, 218].

Finally, it is important to collect accurate and detailed information on patients' physical activity. It would be very useful to steadily monitor, even remotely through new technologies, important parameters such as posture, magnitude, duration, and daily physical activity [219, 220, 221, 222, 223, 224]. It is well known that appropriate foot care, early recognition of patients at high risk, and patient education are considered the most effective weapons for the prevention of foot ulcer or injury [1, 5, 225]. ET treatment may play an important role in each of these three phases.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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