Research Article - Basic and Applied Anatomy

Diabetic foot prevention: the role of exercise therapy in the treatment of limited joint mobility, muscle weakness and reduced gait speed

Piergiorgio Francia[1,*], Roberto Anichini[2], Alessandra De Bellis[2], Giuseppe Seghieri[3], Renzo Lazzeri[1], Ferdinando Paternostro[1], Massimo Gulisano[1]

[1] Department of Clinical and Experimental Medicine, University of Florence, Florence, Italy;
[2] Diabetes Unit, USL 3, Spedali Riuniti, Pistoia, Italy;
[3] Tuscany Regional Health Agency (ARS), Florence, Italy.

Abstract

Objective: It is well known that limited joint mobility of the ankle and foot level, impaired muscular performance and reduced gait speed are risk factors for ulceration in diabetic foot. The aim of this study was to evaluate the effect of an experimental protocol of exercise therapy on joint mobility, muscular strength and gait speed in a group of long-term diabetic subjects.
Methods: The protocol consisted of a 12-week supervised training program; both joint mobility and muscular strength at the ankle were measured before and after exercise therapy respectively by an inclinometer and isometric dynamometers in 26 diabetic subjects and compared to 17 healthy controls.
Results: Ankle joint mobility of plantar flexion was reduced about 36% and dorsal flexion by about 23% in diabetic subjects compared to controls (p<0.001), but significantly increased after exercise therapy (p<0.001 for both). Ankle muscular strength in plantar flexion was reduced by about 51% and in dorsal flexion by 30% in diabetic patients compared to controls, but these also significantly increased after exercise therapy (p<0.001). Consequently, patients' walking speed increased after exercise therapy by 0.28 m/s (p<0.001).
Conclusion: A 12-week supervised program of exercise therapy significantly improves joint mobility, muscular performance and walking speed in diabetic patients--thus limiting one of the pathogenic factors of diabetic foot and potentially preventing disability.

Introduction

Diabetic foot is a major and progressively expanding health problem which often leads to foot ulceration, lower limb amputation and an increased death rate (Boulton et al., 2005). Neuropathy, vasculopathy and infection are known to be the main etiological factors of diabetic ulcers (Boulton, 1991). Nevertheless there are several contributory factors such as limitation of joint mobility, muscle weakness, gait abnormalities, and foot deformities that altogether are responsible for turning a normal foot

___

* Corresponding author. E-mail: piergiorgio.francia@unifi.it.

___

into one characterized by a major risk of ulceration (Fernando et al., 1991; Cavanagh et al., 1992, 1993; Andersen- et al., 2004a; Giacomozzi et al., 2008; Andersen, 2012; Apelqvist, 2012).

Subjects affected by diabetes have muscular weakness, a deficit of balance and reduced mobility at the ankle, subtalar and first metatarsophalangeal joints which interfere with normal rollover of the foot during the gait, leading to orthostatic posture and walking abnormalities. All these factors may cause an abnormal distribution of plantar pressure and consequently lead to a higher risk of foot ulceration (Salsich et al., 2000; Andersen et al., 2004b; Zimny et al., 2004; Rao et al., 2007; Francia et al., 2014).

Limited joint mobility is widespread in diabetic patients and has an insidious onset followed by asymptomatic progressive deterioration (Campbell et al., 1985; Delbridge et al., 1988; Abate et al., 2011).

The range of motion deficit in diabetic patients' joints is due to periarticular limitations of the muscles, tendons, joint capsules, ligaments, and skin (Abate et al., 2013). A reduction in the range of motion in the affected joints can occur in just a few years after diagnosis, even in young patients (Campbell et al., 1985; Abate et al., 2013; Francia et al., 2013). At the same time it is well known that there is a significant correlation between the range of motion of the foot joints and that of the ankle (Campbell et al., 1985; Delbridge et al., 1988; Zimny et al., 2004).

There are important relationships between polyneuropathy and muscle weakness, both leading to decreased muscle strength and leg muscle atrophy (Van Schie et al., 2004; Andreassen et al., 2009). Recently, type 2 diabetes *per se* has been shown to be associated, often permanently, with an accelerated loss of muscle strength and quality, determining early disability and worsening the patient's quality of life (Park et al., 2007).

On these premises, the aim of this study was to design an experimental protocol of exercise therapy for subjects with longstanding diabetes mellitus, reduced joint mobility and impaired muscular performance, and to evaluate the effect of this training program on patients' muscular strength and joint mobility.

Patients and Methods

Twenty-six diabetic subjects (13 males, 13 females, mean age 62.0, standard deviation 8.2 years) and 17 healthy controls subjects (6 males, 11 females, mean age 58.9, standard deviation 9.6 years) were included in the present study. Patients attending the Diabetes Unit in Pistoia General Hospital were invited to take part in the study and an informed written consent was obtained from all patients and control subjects.

The patients were included in the study if the metabolic control of their diabetes was acceptable and in the absence of significant contraindications to the performance of physical activity, among which was the presence of foot ulcers. The control group was composed of healthy subjects matched for age without any mobility problems. Detailed clinical characteristics of the study participants are shown in Table 1.

Physical examination of study subjects included foot inspection, evaluation of foot deformities and assessment of neuropathy by measuring vibration perception threshold, touch sensitivity with 10 G Semmens Weinstein monofilament, patellar and ankle reflexes.Vasculopathy, peripheral pulses and transcutaneous oxygen tension ($TcpO_2$)

Table 1 – Characteristics of patients and controls. Values are mean ± standard deviation.

Baseline evaluation	Diabetic subjects	Controls
Number	26	17
Age (years)	62.0±8.2	58.7±9.6
Gender (male/female)	13/13	6/11
BMI (kg/m²)	28.3±2.3	28.1±3.2
Type of diabetes (1/2)	7/19.	
Diabetes duration	19.2±9.2	
HbA1c before exercise therapy	7.92±0.62	
HbA1c after exercise therapy*	7.44±0.58	

*P <0.01 compared to before exercise therapy

were evaluated at baseline. Hemoglobin A1c was measured at baseline and at the end of the study using HPLC. The study was approved by the ethics committee of the authors' hospital.

Determination of joint mobility

Joint mobility, determined by the range of motion (ROM) which is defined as the movement of a joint from full flexion to full extension, was measured at the ankle by an inclinometer (Fabrication Enterprises Inc., White Plains, NY, USA) (Draper *et al.*, 1988). The patient was supine, with the ankle joint in a neutral position and the feet over the edge of the bed. The knee corresponding to the ankle to be evaluated, was extended and put over a rigid support 5 cm high. The maximum range of dorsal and plantar flexion was determined after drawing with a demographic pen the fifth metatarsal bone and positioning the inclinometer along the diaphysis of the bone, with one extremity put on the distal condyle, as previously described (Zimny et al., 2004). All measurements were performed by the same observer, who recorded the mean of three consecutive readings.

Determination of muscular strength

The maximum isometric muscular strength in plantar flexion and dorsal flexion was measured in Newtons using two isometric dynamometers and digital weight indicators (Kollock et al., 2010). The first dynamometer was used to measure the plantar flexion strength, and the second to measure the dorsal flexion. The isometric dynamometers were fixed to the wall to allow the patient to be in the correct position and avoid the negative effects of limited joint mobility on the measurement.

To measure plantar flexion the patient was seated on an appropriate bench (Figure 1). The patient's lower limb under examination was resting on the bench with the hip flexed to approximately 90°, the knee almost fully extended and resting on a 5-cm high support. The patient's foot under examination was over the edge of the bench and resting on the dynamometer, with the ankle joint in a neutral position. The patient's con-
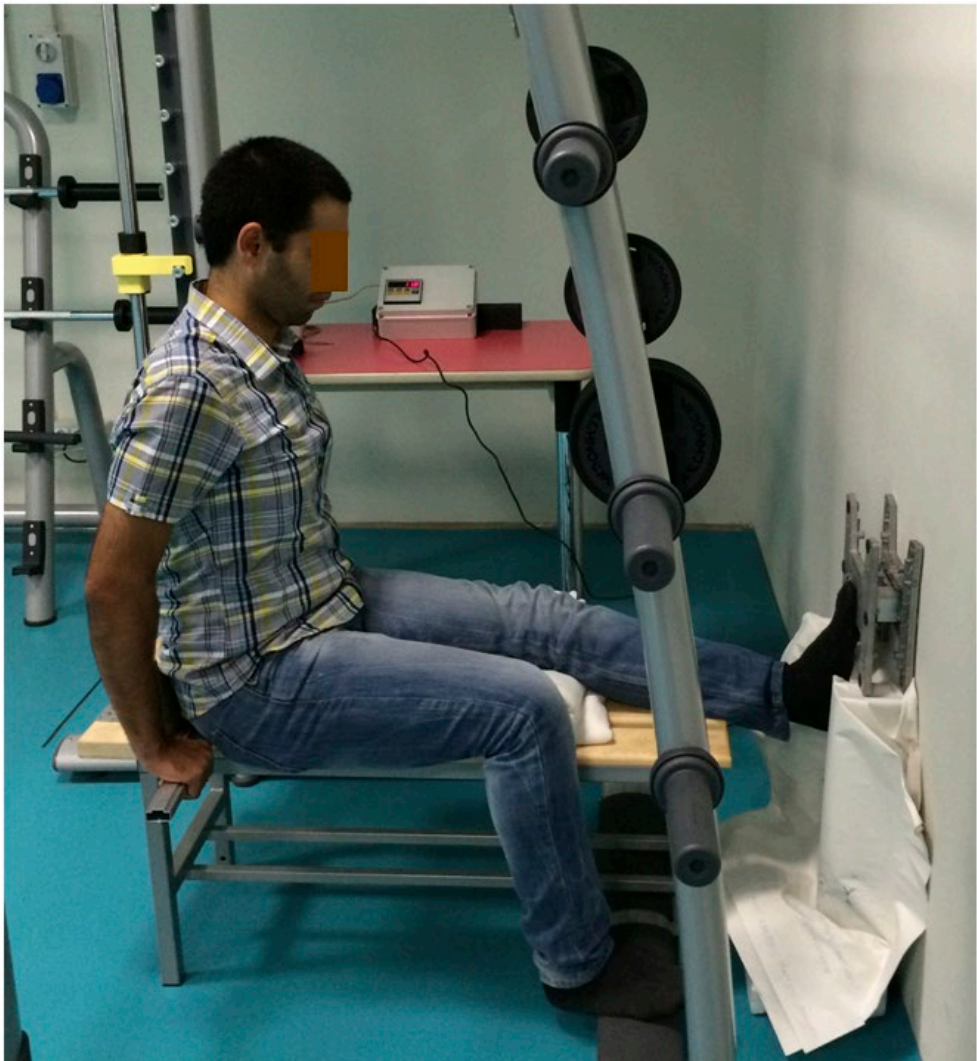
Figure 1 – Position taken by diabetic patients and control subjects during evaluation of maximum isometric muscle strength in ankle plantar-flexion.

tralateral limb was resting with one foot on the floor, positioned forward from the ipsilateral knee. A rigid support of 12 cm height was placed on the dorsal surface of the pelvis in order to create the most stable position during the pushing movement.

To measure ankle dorsal flexion a traction dynamometer was used. Patients were seated as previously described but with one foot on the floor positioned behind the ipsilateral knee while the contralateral knee was held stationary on the 5-cm high rigid support (Figure 2). All the measurements were performed by the same observer and the means of three readings were reported.
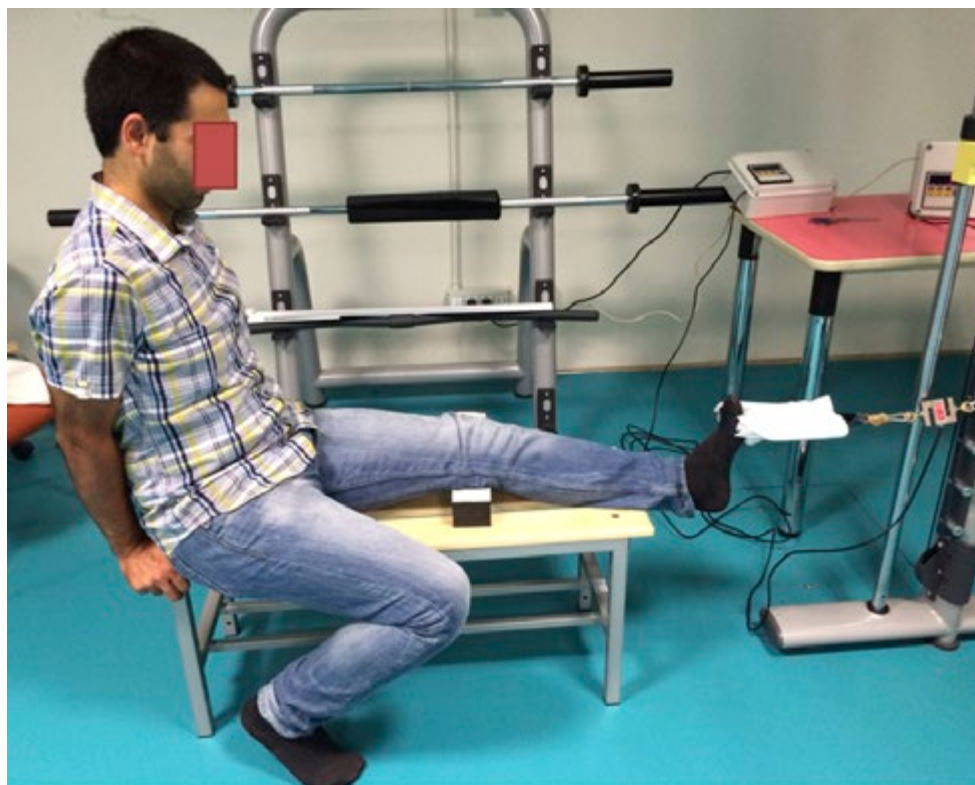
Figure 2 – Position taken by diabetic patients and control subjects during evaluation of maximum isometric muscle strength in ankle dorsal-flexion.

The 10 m walking test

In this test all participating subjects were requested to walk as fast as possible for 10 meters as described in detail elsewhere (Jackson et al., 2008). A "flying start" was used where the subject could accelerate for 2 meters before entering the 10-meter zone, and then decelerate afterwards. The patient's speed was calculated only for the 10 m distance included between the "start zone" and the "end zone", from the time spent walking through that zone. Each subject repeated this exercise three times which were recorded by Stopwatch RS 800 SD (Polar Electro Oy, Kempele, Finland).

Exercise protocol

Diabetic patients participated in a 12-week training program on 3 non-consecutive days a week. The training program was scheduled in such a way that patients could perform it at home according to the proper instructions of a therapist. Every week the diabetic subjects performed the training program in the presence of a therapist in order to check the way they did the physical activity and exercises during the week.

Table 2 – Phases of exercise therapy

Phases	Aims of exercises	Weeks	Minutes
First phase	Warm-up	12	10
Second phase	Stretching muscles and tendons	12	25
Third phase	Improving proprioceptive sensitivity, balance, posture and walking	Last 8	15
Fourth phase	Muscle toning	Last 6	10
Fifth phase	Cool down	12	5

A "training form" with a full explanation of the way in which exercises had to be recorded was given to all patients.

In order to maintain diabetic patients' appropriate metabolic control, avoid the risks associated with physical activity and training drop-out due to altered blood glucose levels, patients were informed of the risk and prevention of hypoglycemia during, immediately after and for several hours following physical training. Patients' blood glucose levels were checked 2 hours before, at the beginning and at the end of the physical activity program.

The training program consisted in a first phase of warm-up: walking or cycling for 10 minutes (Table 2). The stationary bicycle saddle was positioned at a height so that when the patient's foot reached the lowest point of the pedal stroke, his/her knee was flexed by 30°. During warm-up the bicycle saddle was lowered by 3 inches, and the patient's position on the seat was moved forward in order to induce greater ankle dorsal flexion.

The second phase of 25 minutes consisted in stretching muscles and tendons. The exercises were related to muscle and tendon structures of the spine, pelvis and lower limbs, performed while sitting and standing by step, wall bars and elastic bends. Program exercises included the following.
1. While sitting on the bench with feet on the ground resting on a soft mat (without shoes) the patient lifts the heels from the ground, keeping the toes touching the ground to achieve dorsiflexion of the metatarsophalangeal joints. In the same position, the patient rests the dorsal surface of the toes on the ground and exerts ankle and metatarsophalangeal plantar flexion.
2. In the same position, the patient performs ankle plantar flexion with shoes on and the tip of the shoe on the ground while resting. The patient holds elastic bands with both hands and passes them under the plantar surface of the foot to exert foot dorsal flexion, inversion, eversion, pronation and supination.
3. In another exercise, the patient is seated near the end of the bench with knees crossed, puts the elastic band around the ankle and with the closest hand pulls the foot upward to stretch the quadriceps. Then the patient keeps the lower limbs close together while lying on the bench with an elastic band around the foot plantar surface at metatarsophalangeal joint level, and pulls the elastic band while at the same time making ankle dorsiflexion and trunk flexion.
4. The same exercise is repeated with one foot on the ground. The patient keeps the same position without the elastic band, keeping shoulders against the wall, gradu-

ally moving the pelvis toward the wall while sliding along the bench.

5. In another exercise, the patient stands with both hands on the wall bars, puts one foot forward, keeping the feet straight forward and the heel on the ground, leans forward onto the front leg so as to feel the stretching of the calf muscle.

6. In the same position, the patient puts one foot slightly behind, resting on the tip, pushes forward and down on the ankle, trying to extend the knee.

7. While standing on a step with one foot slightly behind and off the step, the patient transfers his/her body weight onto the back heel by pushing it lightly onto the ground to obtain an ankle dorsal flexion.

Patients were required to perform a 20-second stretching followed by 20 seconds of relaxing, twice for each session. They were to rest for 1 minute in between the different exercises. Patients were then instructed to stretch and relax their muscles as they felt muscle tension without pain and thorough relaxation.

A third phase of 15 minutes, during the last 8 weeks of the program, consisted in exercises to stimulate the patient's proprioceptive sensitivity, postural control and orthostatic-dynamic balance. The protocol consisted of the following.

1. The patient was seated on the bench, trying to keep the fingers always in dorsal flexion while slowly sliding the plantar surface over the "sensory roll" from the toe to the heel and conversely with the foot in a normal, pronation and supination position.

2. The patient was to perform frontal – lateral normal and high knee walks at different speeds in a straight line.

3. In front of the mirror, the patient was to stand with both hands lightly supported on the wall bars to avoid falls, then stand on the heel, stand on one leg and do a foot rollover from the toe to the heel and conversely; then to repeat exercises with eyes open and eyes closed, with and without an unstable platform.

Patients were required to perform the exercise for 20 seconds followed by 20 seconds of relaxing twice for each session. When a subject carried out the protocol correctly, the difficulty of the exercises was progressively increased.

The fourth 10-minute phase, during the final 6 weeks, consisted in strengthening exercises for different muscular groups, as follows.

1. The patient was to stand with both hands on the wall bars and perform forefoot lifting, semi-squatting, forward and side lunges.

2. The patient was to lie on the ground, keeping the feet resting on the ground, near the pelvis, and with hands on the ground, keeping the lower back flat, slowly let both knees drop together on one side and then go back to the starting position.

3. In the same starting position, the patient was to lift one foot at a time, while resting on the floor and then lift the other.

Each exercise was to be performed with 8-12 repetitions and 1 minute of relaxation in between exercises.

During the cool-down patients were seated so as not to touch the ground with their feet, and used one foot at a time and then both feet to draw in the air the widest possible letters of the alphabet using the hallux. The last step was for patients to be seated on the bench, and do shoulder circles, neck stretches and chin tucks.

After the first 4 weeks of the training program, subjects were asked to rate their perceived exertion during the training program on the Borg scale (Borg, 1990), which is a vertical scale from 6 to 20, in which 6 represents the absence of symptoms, which

provides an individual measurement of the perceived exercise intensity. This is a simple method of rating perceived exertion.

Statistical analysis

The Wilcoxon signed-rank test was used to test case-control differences in strength and mobility, whereas repeated ANOVA was applied to calculate any significant changes in before and after the training program for both control and case groups.

Results

Ankle joint mobility in flexion and extension was significantly lower in basal conditions in diabetic subjects compared to control subjects, (p<0.001), but after the period of exercise therapy this mobility was significantly increased (Table 3; p<0.001).

Table 3 – Ankle joint mobility in diabetic patients before and after exercise therapy and in control group at baseline. Values are mean ± standard deviation.

ROM*	Controls	Diabetic patients before exercise therapy	Diabetic patients after exercise therapy
Right ankle plantar flexion	21.17±4.20	13.62± 4.62	19.60±3.99
Left ankle plantar flexion	18.54±3.41	12.76± 4.88	20.07±4.62
Right ankle dorsal flexion	46.76±8.20	36.72±11.89	46.35±8.72
Left ankle dorsal flexion	47.29±9.52	35.20±11.35	44.01±7.86

*ROM = range of movement, in degrees
Diabetic patients before exercise therapy vs diabetic patients after exercise therapy: p<0.001
Diabetic patients before exercise therapy vs. controls: p<0.001
Diabetic patients after exercise therapy vs. controls: NS

Table 4 – Muscle strength in ankle plantar and dorsal flexion in diabetic patients before and after exercise therapy and in controls at baseline. Values are mean ± standard deviation.

Strength (Newton)	Control group	Diabetic patients before exercise therapy	Diabetic patients after exercise therapy
Right ankle plantar flexion	906.25±236.13	439.78±196.00	840.03±252.41
Left ankle plantar flexion	866.03±253.69	391.03±186.26	784.90±252.71
Right ankle dorsal flexion	237.50± 78.48	166.48± 78.58	223.96± 84.17
Left ankle dorsal flexion	231.32± 84.56	156.76± 67.89	215.72± 71.32

Diabetic patients before exercise therapy vs. diabetic patients after exercise therapy: p<0.001
Diabetic patients before exercise therapy vs. controls: p<0.001
Diabetic patients after exercise therapy vs. controls: NS

Muscular strength at the ankle in plantar and dorsal flexion was significantly lower in basal conditions in diabetic subjects versus controls (Table 4; $p<0.001$), but this strength significantly increased in diabetic subjects after the period of exercise therapy, achieving on average values similar to those measured in the control group ($p<0.001$).

Before the training period, the gait speed of diabetic patients was significantly reduced compared to controls (1.65 m/s vs. 1.95 m/s, $p<0.002$). However, this gait speed was significantly improved after the treatment period ($p<0.001$) in the diabetic group and achieved a value similar to that of controls. The results of the perceived exertion, as measured by the Borg scale, have shown that this activity was considered moderate with an average mean value of 11.81 ± 2.94. The hemoglobin A1c of diabetic subjects decreased during the treatment period (Table 1; $p<0.01$).

Discussion

Limited joint mobility and reduced muscular strength are very common in diabetic patients, even in the absence of diabetic complications. Interestingly, it has been shown that adults affected by diabetes have an accelerated loss of skeletal muscle strength (Park et al., 2007), strongly suggesting that low muscle strength in diabetic adults is a consequence rather than just a coincidence of the disease. These characteristics may explain the difficulty that diabetic patients have in performing physical activity which then leads to the development of further physical disability. Muscle quality also declines more rapidly in adults with diabetes (Andersen et al., 2004b), suggesting that diabetes can result in functional impairment of muscular tone of the lower extremities.

The mechanisms behind the rapid loss of skeletal muscle strength in older adults with diabetes are not known. There is some evidence that reduced muscular strength and muscular atrophy occur in the presence of neuropathy (Andersen et al., 1996), as well as with the increase in inflammatory cytokines, such as TNF-alpha and IL-6, all of which have negative effects on muscle mass, strength and physical performance in older adults (Visser et al., 2002; Cesari et al., 2004; Del Rosso et al., 2006).

In the presence of low joint mobility the foot is unable to correctly provide shock absorption and may lose its ability to maintain normal plantar pressure. This effect may facilitate trauma in the plantar surface and ultimately lead to foot ulceration (Zimny et al., 2004). In this context exercise has always been considered an important component of prevention and therapy (Colberg et al., 2010). There is strong evidence supporting the effectiveness of regular physical activity in the primary and secondary prevention of several chronic diseases including diabetes, especially in previously sedentary individuals (Warburton et al., 2006).

Moreover, leg muscle ultrasonography studies have suggested that diabetic patients - before exercise therapy - show a qualitative difference between connective and muscular tissue compared with controls. Ultrasonographic images suggest that the ratio between connective and muscular tissue and muscle quality can be improved after exercise therapy (Anichini et al., 2008).

Exercise therapy, in addition to playing an important role in limiting the negative factors involved in the pathogenesis of diabetic foot, is vital to the maintenance of

basic physical function and prevention of disability. Diabetic patients are often unable to perform physical activity, especially if they are elderly and have previously had a sedentary lifestyle (van Schie, 2008).

In keeping with these observations, our findings demonstrate that a period of 12 weeks of exercise therapy which is tailored to the subject's condition, is able to improve ankle joint mobility, muscular strength and walking performance. It is evident that the decline in musculoskeletal fitness of diabetic patients, which often results in disability, may be reversible. The improvement we have seen in our patients' performances after exercise therapy can enhance their capacity to meet the demands of everyday life and to allow them to maintain functional independence, with the additional benefit of improving the control of their disease. Our study also demonstrates the effectiveness and feasibility of an exercise program in diabetic patients, suggesting that such programs should be offered as routine therapy together with nutritional counseling and medication.

In conclusion, in agreement with other recently published data showing improved balance and gait in diabetic subjects after tailored training, (Balducci et al., 2010, 2012; Francia et al., 2014, Morrison et al., 2012) our findings demonstrate the role of a supervised exercise program in the treatment of diabetic patients at risk of diabetic foot. It is essential that subjects, after a suitable training program, become able to perform physical activities by themselves, even at home (Collins et al., 2011), since a key role in diabetic foot prevention is the continuous performance of exercise therapy.

Acknowledgments

References

Abate M., Schiavone C., Pelotti P., Salini V. (2011) Limited joint mobility (LJM) in elderly subjects with type II diabetes mellitus. Arch. Gerontol. Geriatr. 53: 135-140.

Abate M., Schiavone C., Salini V., Andia I. (2013) Management of limited joint mobility in diabetic patients. Diabetes Metab. Syndr. Obes. 7: 197-207.

Andersen H. (2012) Motor dysfunction in diabetes. Diabetes Metab. Res. Rev. 28: 89-92.

Andersen H., Poulsen P.L., Mogensen C.E., Jakobsen J. (1996) Isokinetic muscle strength in long-term IDDM patients in relation to diabetic complications. Diabetes 45: 440-445.

Andersen H., Gjerstad M.D., Jakobsen J. (2004a) Atrophy of foot muscles: a measure of diabetic neuropathy. Diabetes Care 27: 2382-2385.

Andersen H., Nielsen S., Mogensen C.E., Jakobsen J. (2004b) Muscle strength in type 2 diabetes. Diabetes 53: 1543-1548.

Andreassen C.S., Jakobsen J., Ringgaard S., Ejskjaer N., Andersen H. (2009) Accelerated atrophy of lower leg and foot muscles - a follow-up study of long-term dia-

betic polyneuropathy using magnetic resonance imaging (MRI). Diabetologia 52: 1182-1191.

Anichini R., Francia P., De Bellis A., Lazzeri R. (2005) Physical activity and diabetic foot prevention. Diabetes 54 (suppl. 1): A50.

Apelqvist J. (2012) Diagnostics and treatment of the diabetic foot. Endocrine 41: 384-397.

Balducci S., Zanuso S., Nicolucci A., De Feo P., Cavallo S., Cardelli P., Fallucca S., Alessi E., Fallucca F., Pugliese G. (2010) Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: a randomized controlled trial: the Italian Diabetes and Exercise Study (IDES). Arch. Intern. Med. 170: 1794-1803.

Balducci S., Zanuso S., Cardelli P., Salerno G., Falluca S., Nicolucci A., Pugliese G. (2012) Supervised exercise training counterbalances the adverse effects of insulin therapy in overweight/obese subjects with type 2 diabetes. Diabetes Care 35: 39-41.

Borg G. (1990) Psychophysical scaling with applications in physical work and the perception of exertion. Scand. J. Work Environ. Health 16 (suppl.): 55-58.

Boulton A.J., Vileikyte L., Ragnarson-Tennvall G., Apelqvist J. (2005) The global burden of diabetic foot disease. Lancet 366: 1719-1724.

Boulton A.J. (1991) Clinical presentation and management of diabetic neuropathy and foot ulceration. Diabet. Med. 8: S52-S57.

Campbell R.R., Hawkins S.J., Maddison P.J., Reckless J.P. (1985) Limited joint mobility in diabetes mellitus. Ann. Rheum. Dis. 44: 93-97.

Cavanagh P.R., Derr J.A., Ulbrecht J.S., Maser R.E., Orchard T.J. (1992) Problems with gait and posture in neuropathic patients with insulin-dependent diabetes mellitus. Diabet. Med. 9: 469-74.

Cavanagh P.R., Simoneau G.G., Ulbrecht J.S. (1993) Ulceration, unsteadiness, and uncertainty: the biomechanical consequences of diabetes mellitus. J. Biomech. 26: 23-40.

Cesari M., Penninx B.W., Pahor M., Lauretani F., Corsi A.M., Rhys Williams G., Guralnik J.M., Ferrucci L. (2004) Inflammatory markers and physical performance in older persons: the InCHIANTI study. J. Gerentol. A Biol. Sci. Med. Sci. 59: 242-248.

Colberg S.R., Sigal R.J., Fernhall B., Regensteiner J.G., Blissmer B.J., Rubin R.R., Chasan-Taber L., Albright A.L., Braun B. (2010) Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care 33: 147-167.

Collins T.C., Lunos S., Carlson T., Henderson K.., Lightbourne M., Nelson B., Hodges J.S. (2011) Effects of a home-based walking intervention on mobility and quality of life in people with diabetes and peripheral arterial disease: a randomized controlled trial. Diabetes Care 34: 2174-2179.

Delbridge L., Perry P., Marr S., Arnold N., Yue D.K., Turtle J.R., Reeve T.S. (1988) Limited joint mobility in the diabetic foot: relationship to neuropathic ulceration. Diabet. Med. 5: 333-337

Del Rosso A., Matucci Cerinic M., De Giorgio F., Minari C., Rotella C.M., Seghieri G. (2006) Rheumatological manifestations in diabetes mellitus. Curr. Diabetes Rev. 2: 455-466.

Draper D.O., Anderson C., Schulthies S.S., Ricard M.D. (1998) Immediate and residual changes in dorsiflexion range of motion using an ultrasound heat and stretch routine. J. Athl. Train. 33: 141-144.

Fernando D.J., Masson E.A., Veves A., Boulton A.J. (1991) Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. Diabetes Care 14: 8-11.

Francia P., Toni S., Anichini R., Gulisano M. (2013) Limited joint mobility in T1DM patients´ life. Pediatr. Diabetes 14: S59-S60.

Francia P., Gulisano M., Anichini R., Seghieri G. (2014) Diabetic foot and exercise therapy: step by step. The role of rigid posture and biomechanics treatment. Curr. Diabetes Rev. 10: 86-99.

Giacomozzi C., D'Ambrogi E., Cesinaro S., Macellari V., Uccioli L. (2008) Muscle performance and ankle joint mobility in long-term patients with diabetes. BMC Muscoloskelet. Disord. 9: 99.

Jackson A.B., Camel C.T., Ditunno J.F., Read M.S., Boninger M.L., Schmeler M.R., Williams S.R., Donovan W.H., Gait and Ambulation Subcommittee. (2008) Outcome measures for gait and ambulation in the spinal cord injury population. J. Spinal Cord Med. 31: 487-499.

Kollock R.O., Onate J.A., Van Lunen B. (2010) The reliability of portable fixed dynamometry during hip and knee strength assessments. J. Athl. Train. 45: 349-356.

Morrison S., Colberg S.R., Parson H.K., Vinik A.I. (2012) Relation between risk of falling and postural sway complexity in diabetes. Gait Posture 35: 662-668.

Park S.W., Goodpaster B.H., Strotmeyer E.S., Kuller L.H., Broudeau R., Kammerer C., de Rekeneire N., Harris T.B., Schwartz A.V., Tylavsky F.A., Cho Y.W., Newman A.B. (2007) Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes: the health, aging, and body composition study. Diabetes Care 30: 1507-1512.

Rao S., Saltzman C., Yack H.J. (2007) Segmental foot mobility in individuals with and without diabetes and neuropathy. Clin. Biomech. 22: 464-471.

Salsich G.B., Mueller M.J., Sahrmann S.A. (2000) Passive ankle stiffness in subjects with diabetes and peripheral neuropathy versus an age-matched comparison group. Phys. Ther. 80: 352-362.

van Schie C.H. (2008) Neuropathy: mobility and quality of life. Diabetes Metab. Res. Rev. 24: S45-S51.

van Schie C.H., Vermigli C., Carrington A.L., Boulton A.J. (2004) Muscle weakness and foot deformities in diabetes: relationship to neuropathy and foot ulceration in Caucasian diabetic men. Diabetes Care 27: 1668-1673.

Visser M., Pahor M., Taafee D.R., Goodpaster B.H., Simonsick E.M., Newman A.B., Nevitt M., Harris T.B. (2002) Relationship of interleukin- 6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. J. Gerentol. A Biol. Sci. Med. Sci. 57: M326-M332.

Warburton D.E., Nicol C.W., Bredin S.S. (2006) Health benefits of physical activity: the evidence. Can. Med. Assoc. J. 174: 801-809.

Zimny S., Schatz H., Pfohl M. (2004) The role of limited joint mobility in diabetic patients with an at-risk foot. Diabetes Care 27: 942-946.