Abstract

Diabetic foot disease is one of the most invalidating long-term complications of diabetes. Given the dramatically increasing prevalence of types 1 and 2 diabetes mellitus worldwide, the medical community must be prepared for the number of diabetic foot ulcers and lower extremity amputations that will follow this “epidemic” of diabetes. In addition to economic costs, the psychological and biosocial aspects of people suffering from diabetes and diabetic foot disease must be considered. Studies have indicated that the implementation of validated guidelines and international standards of diabetic foot care into clinical practice could reduce lower extremity amputation rates by up to 85%. However, in many countries, such a decrease in lower extremity amputation rates is more of an isolated example than a rule. Reduction of the plantar pressure is mandatory for the treatment and prevention of foot ulcers in patients with diabetes and peripheral neuropathy. The recurrence rate of ulcers is extremely high. After ulcer healing, the persisting high plantar pressure during walking causes repeated soft tissue breakdown at each […]

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Clinical Medicine Section  
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WHO Collaborating Centre

Prevention of Diabetic Foot Ulcers:  
From Biomechanics to Therapeutic Patient Education

Thesis submitted to the Medical School of the University of Geneva  
for the degree of Privat-Docent  
by  
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Geneva  
2012
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<tr>
<td>AFPD</td>
<td>Ambulatory foot pressure device</td>
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<tr>
<td>CRP</td>
<td>Critical risk pressure</td>
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<td>DPP</td>
<td>Duration of plantar pressure</td>
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<td>FFC</td>
<td>Foot-floor contact</td>
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<td>FSR</td>
<td>Force sensing resistor</td>
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<tr>
<td>HCP</td>
<td>Health care provider</td>
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<tr>
<td>HRQoL</td>
<td>Health-related quality of life</td>
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<td>LEA</td>
<td>Lower extremity amputation</td>
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<td>LJM</td>
<td>Limited joint mobility</td>
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<tr>
<td>MTS</td>
<td>Metatarsal head</td>
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<tr>
<td>OG</td>
<td>Overlimit gait</td>
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<tr>
<td>PPI</td>
<td>Plantar pressure integral</td>
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<tr>
<td>PPP</td>
<td>Peak plantar pressure</td>
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<tr>
<td>PVD</td>
<td>Peripheral vascular disease</td>
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<td>PWB</td>
<td>Partial weight bearing</td>
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<tr>
<td>TCC</td>
<td>Total contact cast</td>
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<tr>
<td>TDT</td>
<td>Temperature discrimination threshold</td>
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<tr>
<td>THA</td>
<td>Total hip arthroplasty</td>
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<tr>
<td>TG</td>
<td>Total number of gaits</td>
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<tr>
<td>TPE</td>
<td>Therapeutic patient education</td>
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SUMMARY

Diabetic foot disease is one of the most invalidating long-term complications of diabetes. Given the dramatically increasing prevalence of types 1 and 2 diabetes mellitus worldwide, the medical community must be prepared for the number of diabetic foot ulcers and lower extremity amputations that will follow this “epidemic” of diabetes. In addition to economic costs, the psychological and biosocial aspects of people suffering from diabetes and diabetic foot disease must be considered. Studies have indicated that the implementation of validated guidelines and international standards of diabetic foot care into clinical practice could reduce lower extremity amputation rates by up to 85%. However, in many countries, such a decrease in lower extremity amputation rates is more of an isolated example than a rule.

Reduction of the plantar pressure is mandatory for the treatment and prevention of foot ulcers in patients with diabetes and peripheral neuropathy. The recurrence rate of ulcers is extremely high. After ulcer healing, the persisting high plantar pressure during walking causes repeated soft tissue breakdown at each step. In this population, the development of a new walking strategy could alter the plantar pressure distribution under the feet, thus improving patient outcomes and preventing amputation. We have developed and implemented a biofeedback-based technique delivered by an electronic insole. When combined with therapeutic patient education, this method may be a valuable tool for the treatment of foot ulcers and prevention of lower extremity amputations in high-risk patients with diabetes.
INTRODUCTION

Diabetes mellitus is a major health problem worldwide. The occurrence of diabetes has recently reached epidemic levels in both developed and developing countries. Diabetes-related lower extremity complications have a huge impact on the patient quality of life, with enormous economic consequences for individuals and society.

In recent years, the standards of diabetic foot care have improved considerably. However, despite the availability of new treatments, techniques, and advances in the medical and surgical care of people with diabetic foot disease, the incidence of lower extremity amputation in this population is still extremely high. A widening gap exists between our knowledge in the field and the daily experience and outcomes of patients in diabetic foot care centers. The good news is that it is possible to reduce amputation rates by up to 85%.

The remaining question is “How do we do it?”

This work summarizes the considerable effort made in the field of diabetic foot disease. Special emphasis is given to approaches dealing with the issue of the loss of protective pain sensations and its consequences, in terms of the development of at-risk zones under the foot.

The thesis is organized into two parts. The first part describes the global burden of diabetic foot disease, the principal pathological pathways and mechanisms involved in diabetic plantar ulcers, and existing methods for the prevention and treatment of foot ulcers.

The second part presents our contribution to the research in the field, mainly in terms of foot off-loading, linking technology and therapeutic patient education. We focus on the development of a biofeedback-based approach for gait modification and consequent plantar pressure reduction.
PART ONE:

DIABETIC FOOT DISEASE – GENERAL CONSIDERATIONS
Diabetes and diabetic foot disease – the global burden

Diabetes mellitus (DM) is one of the most common noncommunicable diseases globally. It is the 4th or 5th leading cause of death in most high-income countries. The global burden of diabetes is projected to increase from the current 366 million people in 2011 to over 552 million people by the year 2030 (Figure 1). Moreover, about 183 million people have undiagnosed diabetes (1).

![Figure 1: Global projections of the number of people with diabetes (20–79 years), 2011 and 2030 (International Diabetes Federation 2012) (1)](image)

Foot ulcers and amputations are major causes of morbidity, disability, and economic burden for people with diabetes (2). While there is little information available, it seems reasonable to suggest that the clinical problems leading to foot disease and subsequent amputation have a major impact on the quality of life of individual patients.
Diabetes continues to be the leading cause of lower extremity amputations (LEAs) worldwide. Every year, more than 1 million people with diabetes lose a leg as a consequence of their disease. In other words, every 30 seconds a lower limb is lost to diabetes somewhere in the world (2). Approximately 40-60% of all LEAs are related to diabetes and, in some areas of the world, proportions as high as 70-90% have been described (3, 4). It is difficult to estimate the incidence of LEA across countries because of the heterogeneity of study populations.

In the USA, more than 90,000 diabetes-related LEAs are performed annually (5), and there are approximately 300,000 hospitalizations annually for foot cellulitis, ulcers, and deep infections among individuals with diabetes. In Europe, about 250,000 LEAs are performed annually, two-thirds of which are performed in Eastern European countries. In diabetics, LEA incidence represents 50% of all nontraumatic amputations (6), and the age-adjusted risk for LEA is reportedly 15-60 times greater than that of the nondiabetic population (7-9). Furthermore, foot complications are the most common reason for hospitalization in patients with diabetes. Diabetic foot ulcers and LEAs occur in more than 15% of people with diabetes during their lifetime (10, 11). More than half of diabetic amputees require amputation in the contralateral limb within 4 years of losing the first leg (9, 12).

Patients show an elevated mortality rate in the first 3-5 years after an amputation (13), which is often attributed to cardiac or renal complications (14, 15). A recent study in Denmark found a 30-day mortality rate of 30% in a consecutive series of 93 LEAs; more than half of the patients were dead by 1-year postamputation. The mortality rate was significantly related to age and the number of comorbidities (16). Higher overall mortality rates have been reported in diabetic amputees compared to nondiabetic or other diabetic individuals in studies of Pima Indians in Arizona, USA. This population is notable for having the highest amputation rate among diabetic subjects (95% of all amputations were in diabetic subjects) (17).
Reducing the incidence of lower extremity amputations

The relationship between diabetes and LEA is well established, and strategies to reduce the incidence of amputation have been in place for decades. Nevertheless, globally, a corresponding reduction in amputation rates has not been seen. For example, LEA was chosen as a major endpoint by the 1989 St. Vincent Task Force, with a 50% reduction in LEA chosen as the 5-year target (18). After 10 years, although this target was achieved in some centers and by some individual teams in the European region, it was not achieved in many areas due to various obstacles.

A report from one health care district in the UK showed a 50% increase in amputations between 1990 and 1994 (19), whereas a study from Germany found no change between 1990 and 1995 (20). Amputation rates are still increasing in diabetic patients, even while they decrease among those without diabetes (5). When directly comparing population studies, it is important to analyze the specific definitions used and the beliefs of the patients and investigators (21, 22). Otherwise, it can be difficult (or even impossible) to compare rates directly, due to heterogeneity in the study populations. For example, in England, one study found no change in the incidence of major amputation in a mixed-diabetic and nondiabetic population between 2003 and 2008 (incidence of 5.1 per 10^5) (23), whereas another study found a reduction of nearly 50% in patients with type 1 DM (from 1.3 x 10^5 in 1996 to 0.7 x 10^5 in 2005) (24).

Implementation of consensus guidelines

A recently published study from Sweden (25) evaluated the effects of the implementation of consensus guidelines on foot care. They observed a 60% reduction in the rate of above-ankle LEAs performed between 2001 and 2006, whereas the number of minor amputations remained stable. In the cited study, all personnel involved in diabetic foot treatment received education, including lectures and practical training for specialized foot care (25).
Health care provider (HCP)-oriented educational programs have shown beneficial effects on the clinical care of patients with at-risk feet. We showed that holding a common consultation, which patients and their HCPs attended together to observe and learn specialized foot care, had a positive impact on the prevention of foot ulcers in a long-term care facility (26). Another study demonstrated a 48% reduction in LEAs when comprehensive guidelines for diabetic foot management were adapted and systematically implemented by primary care clinicians in their practices (27).

More recently, data from a nationwide statutory health insurance database in Germany from 2005 to 2007 were used to identify a standardized relative risk of 8.8 (7.3-10.7) in men and 5.7 (4.3-7.6) in women for a first nontraumatic lower-limb amputation (28). This meaningful reduction in the incidence of diabetes-related LEAs could be related to a significant improvement in the organization of diabetes care (29). In the South Tees area in the UK, over a continuous 5-year period (1995-2000), the relative risk of a person with diabetes undergoing a diabetes-related LEA went from being 46 times that of a person without diabetes to 7.7 at the end of the 5 years (30). At a time when major non-diabetes related LEA rates increased, major diabetes-related LEA rates have fallen.

The “Healthy People 2000” initiative in the USA called for a significant reduction in LEAs, aiming for a 40% reduction in LEA rates by the year 2000 (31). However, according to the American Veterans Administration System, despite an average 5% decrease in major and minor amputations per year between 1989 and 1998, data from the diabetic population alone showed no significant reduction in amputations over the 10-year period (32). The incidence of LEAs has become the focus of renewed interest by the medical profession and political bodies. New initiatives, including the “Putting Feet First” campaign in the UK (33) and the “lower limb salvage” theme of international meetings, have been launched to raise awareness and to reduce the incidence of amputation (34).
The aforementioned decreases in LEA rates from population-based studies (28, 30) are isolated examples rather than the norm. Large studies from different countries are needed to confirm the actual trend of the incidence of LEA in patients with DM.

**ECONOMIC CONSIDERATIONS**

The costs related to diabetic foot disease and limb amputations are high. Economic cost in terms of money, as well as psychological and social costs, must be considered. The available health economic studies mostly analyze and reflect the economic consideration for society. Comparison of costs associated with amputations in different studies are difficult to make because of differences in the study designs, patient populations, types of foot lesions, health care systems, treatment practices, time frames for analysis, study perspectives, reimbursement systems, and countries included (35). These studies usually only consider the direct costs for the healthcare system. The calculations must include all costs incurred, including investigations, treatments, hospitalizations, outpatient visits, local wound treatment until the wound is completely healed, and rehabilitation. Indirect costs of morbidity and mortality related to foot ulcers and amputations should also be considered. These costs could include the value of productivity losses when patients are unable to work or when they die prematurely as a result of their foot lesions or associated complications.

The cost often does not consider the differences between costs of foot-related complications and complications for diabetic patients in general. A study showed that other conditions were reported as the primary diagnoses in more than 80% of discharges in which diabetic foot complications were actually the main reason for hospitalization (36). This finding clearly demonstrates the underestimation of costs related to diabetic foot lesions when analyses are based on primary diagnoses from secondary data sources.
Quality of life – what is the cost after amputation?

Lower extremity amputations have a major impact on the quality of life of patients and their families. According to one study, although patients with a minor amputation (e.g., toe) had a quality of life equal to that experienced by patients with a healed ulcer, patients with a major amputation (e.g., transtibial) had a quality of life index that was reduced by about 50% (37). In another study (38), the health-related quality of life (HRQoL) of patients with chronic diabetic foot disease, even without amputation, was poor and comparable to that of patients with recurrent cancer (39). A more recent article showed that ulcer healing was associated with improvement of HRQoL; however, patients with active ulceration reported poorer HRQoL scores than those who had undergone successful minor LEA (40).

In the elderly (age ≥ 80 years), amputations have even more negative outcomes. The mortality risk of a major LEA in elderly patients was observed to be 50% in less than 2 years, and 55% of these patients showed a worsened ability to function independently after the operation. Whereas preoperatively, most subjects walked independently or with an assistive device, postoperatively they often required a wheelchair or were bed-bound for extended periods. Only 5% of patients improved their functional status score after amputation (41).

Economic costs of diabetic foot disease

In most countries, 25% to 50% of the cost for the inpatient care of diabetes is attributable to the diabetic foot (42-44). Two Swedish studies found the costs of topical treatment and outpatient stays to be the most substantial (45, 46). Healing of a single ulcer costs approximately $17,500 (35). The time needed for complete wound healing after an amputation in patients with diabetes is variable and depends on the level of amputation. The mean healing time for patients with minor or major amputation was shown to be as long as 52 or 38 weeks, respectively (46).
In the USA, Reiber estimated the total direct costs for amputation to be $20,000 to $25,000 (1992) (47). At approximately the same time, Apelqvist et al. estimated that the cost varied between $43,000 and $65,000 in Sweden, depending on the level of amputation (1994) (45). More recently, this cost was found to vary from about $30,000 to $33,500 in Sweden (2004) (35). In the USA, the average inpatient cost for toe/transmetatarsal amputations was $25,241, transtibial amputations was $31,436, and transfemoral amputations was $32,214 (2002) (48). Long-term costs, including prostheses, special footwear, rehabilitation costs, costs for home care and social services, and costs related to any residual disability and productivity losses, must also be considered.

Given the high costs of diabetic foot disease, however calculated, to individuals and society, preventive foot care and low-cost interventions will almost certainly be effective. Interestingly, the cost of a minor amputation (e.g., of an infected phalanx or metatarsal head), including a short 3-day hospitalization, is less than the cost of the purely conservative approach of medical treatment encompassing 6 weeks of at-home intravenous antibiotic therapy (49). This kind of economic consideration is fully accepted by some health insurance companies, and is very nicely reflected by George Bernard Shaw (1856-1950, Nobel Prize award for literature in 1925), who said:

“I marvel that society would pay a surgeon a large sum of money to remove a person’s leg – but nothing to save it.”

The reimbursement system may be one of the most dangerous enemies of the diabetic foot (50, 51). If the cost of a surgical amputation procedure is reimbursed but those of outpatient care and preventive strategies (e.g., foot care, protective shoes) are not, then the incidence rate of LEAs may continue to increase. In many European countries, most people are assured affordable governmental health care. In the USA, costs are more often paid by the patient or insurance company.
DIABETIC FOOT DISEASE: CAUSAL PATHWAYS

Perhaps nowhere in the body do we see so plainly the ravages of the diabetic complications of neuropathy and vascular disease as in the foot. These common and often disabling foot problems lead to suffering, disability, time lost from work, hospitalization, and great expense to the patient and the community. The primary approach to the problem must begin with an understanding of the basic metabolic abnormalities of diabetes: not only insulin, carbohydrate, and lipid abnormalities, but also the pathological processes that could develop in the blood vessels and nerves.

![Causal pathway to diabetic foot ulceration](adapted from Pecoraro R.E. et al. Diabetes Care 13:513-21, 1990 (52))
1. Diabetic peripheral neuropathy

The most important factor involved in diabetic foot disease is peripheral neuropathy (Figure 2). Symptoms of neuropathy were mentioned by Aretaeus (as early as ca. 50 AD) in his classical description of diabetes as a disease (53). The first clinical description of diabetic neuropathy was made by Rollo in 1798, who described a patient with “pain and paraesthesia” (54). The syndrome was described in more detail during the 19th century, but it was not until 1945 that the first comprehensive description of this disorder was published (55).

Diabetic neuropathy is an umbrella term encompassing 2 distinct groups of disorders, focal and diffuse neuropathies, with different etiologies, progressions, and treatments. A detailed definition of diabetic neuropathy was agreed on at the 1988 San Antonio Consensus Conference: “a demonstrable disorder, either clinically evident or subclinical, that occurs in the setting of diabetes mellitus without other causes for peripheral neuropathy. This definition includes manifestations in the somatic and/or autonomic parts of the peripheral nervous system” (56). The mere association of neuropathic symptoms with DM is insufficient for the diagnosis of diabetic neuropathy, and other causes of peripheral neuropathy that might be treated differently or have a different prognosis must be excluded.

The definition provided by the World Health Organization focuses on the clinical picture of diabetic polyneuropathy as including the “progressive loss of nerve fibers leading to sensation loss [and] foot ulceration.” This definition underlines the natural history of diabetic neuropathy and the absolute necessity for the physician to intervene and set up measures of secondary and tertiary prevention to avoid foot complications and, in particular, amputation (57). This definition is based on the fact that the late sequelae of peripheral neuropathy include foot ulceration, Charcot neuroarthropathy, and amputation, although many of these complications are potentially preventable (58). Boulton et al. (59) defined diabetic polyneuropathy as the “presence of symptoms and/or signs of peripheral nerve
dysfunction in people with diabetes after exclusion of other causes”. Finally, the Neurodiabetes Consensus (Toronto) Group on diabetic polyneuropathies supports the earlier classification into generalized, focal, and multifocal, and further separates diabetic polyneuropathy into typical and atypical neuropathies (60).

The most common form of neuropathy affecting individuals with diabetes is diffuse chronic sensorimotor peripheral neuropathy (61). Neuropathic ulceration is a complication of distal neuropathy that occurs predominantly in individuals with loss of protective pain sensation.

**Prevalence of diabetic neuropathy**

Available data concerning the incidence and prevalence of peripheral neuropathy differ considerably, partially because of the lack of a consensus on the basic definition and classifications of diabetic neuropathy, as well as differences in patient selection and diagnostic procedures among studies. Accordingly, reported prevalence rates vary between 5% and 100% (62-67). Studies reporting 100% prevalence rates have all been based on nerve conduction experiments (68). Diabetic neuropathy has been shown to be present in more than 50% of persons with diabetes who are older than 60 years (63).

Among 3 large, clinic-based studies from Europe, the prevalence of diabetic polyneuropathy varied from 23% to 29% (63, 69, 70). More recently, the Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes (BARI 2D) study found that the prevalence of diabetic peripheral neuropathy was 51% (71). The much-cited study of Pirart (72) was both large and long-term (4,400 cases followed for up to 25 years). This study found evidence of neuropathy in 8% of patients at diagnosis. After 25 years of diabetes, 50% of patients had objective signs of neuropathy, defined as abnormal reflexes and vibratory sensation. The Rochester neuropathy study had a prevalence rate for diabetic neuropathy of 50%, with 15% having clinical neuropathy (64). A cross-sectional study of more than 6,400
hospital-based diabetic patients found a 29% prevalence of clinical neuropathy, which was defined on the basis of a disability and symptom score (63).

Diabetic peripheral neuropathy has 3 principal components: motor, sensory, and autonomic (Figure 2).

1. The motor component leads to small-muscle wasting, with a consequent imbalance of flexor and extensor muscles, leading to foot deformities (clawing of the toes and prominence of the metatarsal heads). These foot deformities result in alterations of the foot shape, which could be associated with subluxation at the metatarso-phalangeal joints. This condition leads to anterior displacement of the submetatarsal fat pads and reduced subcutaneous tissue thickness at the metatarsal heads (73), resulting in abnormal plantar pressure.

2. Sensory deficit and symptoms, which generally predominate over motor involvement, appear first in the most distal portions of the extremities and progress proximally in a “stocking-glove” distribution (74). The signs, symptoms, and neurologic deficits of distal symmetric sensorimotor polyneuropathy vary, depending on the classes of nerve fibers involved. The larger, faster, myelinated type A nerve fibers are associated mainly with proprioception, light touch, pressure sensation, vibration perception, and motor nerves to the muscle spindles. Loss of this nerve fiber type diminishes light touch and proprioception, the latter resulting in ataxic gait and unsteadiness, as well as weakness of intrinsic muscles of the feet (and hands) (74). This so-called “pseudotabes” form of neuropathy resembles the neuropathy seen in tabes dorsalis. The smaller, slower, unmyelinated type C fibers are associated with free nerve endings, which appear to have a particular role in the detection of noxious, painful, and thermal stimuli (75).

3. Peripheral autonomic neuropathy is often found in association with somatic polyneuropathy and may occur at an earlier stage, resulting in smooth atrophic skin and
sweating abnormalities of the feet (76). Plantar callus (hyperkeratosis) may be a sensitive indicator of neuropathy (77-79). Loss of sudomotor function may also precipitate cracking of the skin and the formation of fissures, which may become secondarily infected. Another consequence of autonomic neuropathy is autosympathectomy, which could lead to arteriovenous shunting, increased cutaneous blood flow, increased skin temperature, and distension of the dorsal veins in the foot (80, 81).
2. Peripheral vascular disease

Some researchers believe that atherosclerotic vascular disease is probably present in all patients with DM (82). Peripheral vascular disease (PVD), defined as atherosclerosis of the peripheral blood vessels, is 2–3 times more likely to develop in people with diabetes than in the general population (83). The prevalence depends on the definition and the surveyed population. Defined as the presence of intermittent claudication, PVD was reported in the Framingham Study to be 3.8 and 6.8 times more common in diabetic than in nondiabetic males and females, respectively. Age-adjusted incidence rates of claudication per thousand for people with diabetes were 12.6 for men and 8.4 for women (82).

Mayo Clinic data indicated that PVD, defined as peripheral pulse deficit, was present in 8% of subjects at diabetes diagnosis, 15% after 10 years of diabetes, and 45% after 20 years of clinical diabetes (84). In the University Group Diabetes Program (UGDP) study, cumulative incidence rates of nonpalpable dorsalis pedis pulse, intermittent claudication, and arterial calcification were 35%, 38%, and 61%, respectively, in men, and 38%, 24%, and 32%, respectively, in women after diabetes diagnosis (85). Although PVD is more prevalent among the diabetic population, once established it does not progress any more rapidly than does PVD in the nondiabetic population (86). Cross-sectional studies have indicated that about 15% to 30% of patients with type 2 diabetes may have evidence of PVD when studied by noninvasive techniques (87, 88).

In addition to its dependence on the underlying arterial circulation, adequate cutaneous perfusion may also be critically influenced by other factors, including skin integrity, the mechanical effects of repetitive pressure, and tissue edema (89). Proano et al. studied the relationship between weight-bearing pressure and nutritive skin circulation in the plantar region. They concluded that the circulation was arrested at a weight-bearing pressure in the plantar region of 3 N/cm² in both diabetic subjects and controls (89). This result implies that large areas of the sole of the foot, e.g., the plantar aspects of the great toe and of the
metatarsal and heel regions, are subjected to circulatory arrest in the standing position. Brash et al. found that capillary fragility was increased in the feet of neuropathic patients with a history of ulceration compared to those of neuropathic control subjects (90).

According to our results (91), PVD could contribute to elevated plantar pressure and prolonged duration of the foot-floor contact at each step. The principal pathway could be the atrophy of subcutaneous soft tissue or intrinsic muscles in the sole of the foot. Edmonds et al. reported that the plantar soft tissue thickness under the 1\textsuperscript{st} and 5\textsuperscript{th} metatarsal heads was reduced in the neuroischemic foot compared to the neuropathic foot (92). Thus, a vicious circle is established, whereby the elevated plantar pressure contributes to the impaired local circulation that, in turn, leads to soft tissue hypotrophy or atrophy. As a result, an additional increase in plantar pressure could develop.
3. Limited joint mobility

Limited joint mobility (LJM) has been well documented in patients with DM. It was first reported in non-neuropathic diabetic children in 1976 (93), and it is associated with increased pressure, current ulcer, and a history of plantar ulcer (94-98). It is probably due to the nonenzymatic glycosylation of collagen owing to chronic hyperglycemia, which results in stiffening of the joint ligaments and nearby structures (98, 99). Clinically, LJM is manifested as thick, tight, waxy skin and restriction of joint movement (100, 101). A reduction in the available range of motions at numerous joints has been reported in diabetic patients compared to nondiabetic controls (95-97).

Zimny et al. studied LJM at the ankle and 1st metatarso-phalangeal joint in patients with diabetes (n = 35), diabetic polyneuropathy (n = 35), and healthy controls (n = 30) matched for age and body mass index (BMI). In a supine non–weight-bearing position, the polyneuropathy group had significantly less total ankle mobility (17.9° vs. 31° or 28.4°) and 1st metatarso-phalangeal joint mobility (35.3° vs. 59.4° or 62°) than healthy or diabetic controls (97). Fernando et al. found increased plantar pressures under the subtalar and 1st metatarso-phalangeal joint in patients with DM (95). It is generally assumed that LJM increases plantar pressures by restricting pronation at the subtalar joint, based on the traditional understanding of the foot as a “mobile adaptor” (99).
4. Gait alterations

The task of walking is an extremely complex motor control problem. Normal walking requires sensory input to modify learned motor patterns and muscular output to execute the desired action (102). People with diabetes and neuropathy frequently report being uncertain of foot placement during gait (103). Balance and gait require the central integration of afferent information arising from 3 peripheral sensory systems: the vestibular organs, visual apparatus, and somatosensory receptors throughout the body (104). In addition, adequate and accurate motor control is needed to maintain the body in the upright position and to adjust to external destabilizing forces. The neuromuscular damage implied by peripheral neuropathy may result in altered lower extremity biomechanics (105), thereby leading to gait alterations (i.e., modified walking speed and gait pattern, with increased risk of falling).

Cavanagh et al. showed that the control of gait and posture is a clinically significant problem in patients with diabetic neuropathy (106). There is strong evidence that diabetic individuals with neuropathy demonstrate a relative deficit in their ability to maintain posture, even when adequate function of the other sensory organs is present (107). Allet et al. (108) showed that diabetic patients with peripheral neuropathy have more gait alterations than diabetic patients without peripheral neuropathy. Moreover, gait alterations may appear well before peripheral neuropathy is detected clinically (109). Petrofsky et al. (110) reported that patients with diabetes are at a risk of falling before loss of foot sensation. Thus, clinical factors other than neuropathy (109), such as muscle strength (111), joint mobility, general deconditioning, or psychological traits (e.g., fear of fall), may deteriorate gait in diabetic patients.

In a double-blind multicenter study of 1,035 patients, Abbott et al. identified abnormal muscle strength as a predictive factor for foot ulceration. They also suggested that progressive motor weakness and proprioceptive loss may lead to gait abnormalities, which
are major contributory factors to increasing pressures and loads on potential plantar ulceration sites (107). Reduced muscle strength, as determined by foot, knee, and wrist movements, has been related to the presence of neuropathy in long-term type 1 DM patients (112). In such patients, the ability to perceive the exact tension being exerted by muscles of the leg and foot is diminished (106). Given that knee and ankle reflexes are frequently absent in individuals with diabetic neuropathy, several components of the “gait control system” are clearly either missing or degraded in these patients. The absence of sensory feedback may lead to a less variable kinematic pattern during steady-state gait, which may suggest one possible cause for plantar neuropathic ulceration (106).

Recent results confirm that the degree of neuropathy influences walking speed when changing terrains. Neuropathy, together with muscle weakness, could influence the neuromuscular control process. Both may affect not only joint moments and power generation but also the timing of muscle activation and, thus, gait performance (113). However, reduced gait speed could also be an adaptation strategy. It may be that diabetic patients walk slower because of altered neuromuscular control processes leading to decreased balance and stability. The association between participants’ fear of falling and decreased velocity could support this theory. Slowing down might be a security strategy to feel safer on irregular terrains. Nevertheless, reduced walking speed does not necessarily imply increased safety during walking (114). Younger adults improve their dynamic stability by walking slower, whereas older adults fall more often.
5. **Callus and hyperkeratosis**

Keratinization is a normal physiological process that maintains the stratum corneum as a protective cover. Under the influence of intermittent compression, the process of keratinization can be overactivated, resulting in hypertrophy of the stratum corneum, a condition called hyperkeratosis (115).

A callus is a broad-based, diffuse area of hyperkeratosis of relatively even thickness. Plantar callus formation was first associated with diabetic foot ulceration by Murray et al. (77), who prospectively found a relative risk of 11.0 for ulceration in a callused area compared to a noncallused area. Over 100 years ago, Pryce described a diabetic patient who developed an ulcer which “commenced as corns” (116). Many previous studies have suggested that alterations in cell metabolism and in mechanical properties of the skin (102, 117) can predispose patients with DM to callus formation.

Collagen glycosylation results in the thickening and crosslinking of collagen bundles. The clinical result could be thick, tight, and waxy skin (100). It also has been suggested that the epidermis in callosities has a higher rate of cell division than normal plantar skin, and that the resulting cells do not stay within the epidermis for a sufficient time to mature and differentiate fully (118). Moreover, the renewal time of the stratum corneum is longer in the case of callus. Experimentally, Thomas et al. found a renewal time of 26 days for callosities compared to 16 days for normal plantar stratum corneum (118).

Neuropathy may predispose a patient to plantar callus development (100, 119). Peripheral neuropathy and its motor component lead to foot deformities. Denervation of the intrinsic foot muscles and loss of stability due to the unopposed action of the long extensor tendons result in prominent metatarsal heads and anterior displacement of the protective plantar fibro-fatty padding. In other words, these conditions lead to an increase of mechanical stress on the plantar surface, with associated callus formation. Another risk factor for callus
formation in neuropathic patients is autonomic neuropathy, which leads to decreased sweating with consequent anhydrosis, resulting in dry skin that is prone to cracks and fissures. Finally, hyperkeratosis significantly increases plantar pressure. We have shown that diabetic patients with hyperkeratosis have significantly increased peak plantar pressure and duration of plantar pressure values compared to patients without hyperkeratosis (79) (Figures 14 & 15, page 61).
6. High plantar pressure

Most diabetic foot complications resulting in amputation begin with the formation of a skin ulcer. Epidemiological studies have shown that a foot ulcer precedes and is responsible for 85% of all LEAs in the diabetic population (52). Moreover, 94% of diabetic ulcers occur under the area of increased plantar pressure (120).

The principal factor involved in plantar ulcer development and elevated plantar pressure in patients with diabetes is peripheral sensorimotor neuropathy. This complication of diabetes, characterized by a lack of protective pain sensation combined with foot deformities, exposes diabetic patients to undue sudden or repetitive stress that leads to callus and foot ulcer formation (Figure 3).

![Image of foot biomechanics](image)

**Figure 3**: Biomechanics of foot relative to elevated plantar pressure (from Sumpio B.E. N Engl J Med 343:787-93, 2000 (121))

In a review of several studies, Boulton suggested that neuropathy could be implicated as a causative factor in 90% of more than 600 episodes of ulceration (122). Other factors, such as LJM, callus formation, foot deformity, and reduced resistance to infection, also contribute to the causal pathway of skin breakdown and consecutive ulceration (123).
The early recognition and management of risk factors for ulcers and amputations is crucial to prevent or delay the onset of adverse outcomes (2). Most lower extremity complications are easily preventable through educational programs for patients and HCPs (124). An 85% reduction in below-knee amputations through specific foot care teaching and a long-term follow-up program was demonstrated in Geneva (124). There is a demand for additional therapeutic and preventive possibilities to help patients avoid devastating complications of the disease, preferably before a foot ulcer occurs or an amputation becomes imminent in an at-risk population.

Many years ago, Lipsky et al. studied the thermographic patterns of the soles of the feet of normal runners (125). They suggested that each individual developed his/her own pattern of “hot spots” on the sole after running. However, after a further period of running, the normal subject altered his/her gait just enough to spare the now-tender areas of the foot, putting more stress on less-involved parts of the foot.

This constant change of stress patterns on the foot in response to the perception of tenderness and changing thresholds of pain is probably the most important factor to prevent tissue breakdown and ulceration in normal individuals. Persons with peripheral neuropathy do not appear to limp or to change their gait in the early stages of traumatic inflammation. They continue to walk until they develop necrosis, a blister, or an ulcer (125). Bacterial infection, tissue ischemia, continuing trauma, and poor management cause diabetic foot ulcers to heal slowly and to transform into chronic wounds (126).
PREVENTION AND TREATMENT OF DIABETIC FOOT ULCERS

The most important factors related to the prevention and treatment of foot ulcers in patients with diabetes are the consequences of peripheral neuropathy with minor foot trauma. In the absence of protective pain sensation, patients do not accord sufficient importance to any wound on their feet. Many patients only visit a physician when an ulcer is in an advanced phase or already infected. The absence of natural pain-related “feedback” from the injured lower extremity could be considered the most relevant cause of the initial development of most foot ulcers in diabetic patients. An unperceived minor trauma is the precipitating factor of any neuropathic plantar foot ulcer in diabetics.

One preventive modality is therapeutic patient education (TPE), which should be an integrated part of the classical medical approach.
THERAPEUTIC PATIENT EDUCATION AS THE BASIS FOR PREVENTION AND TREATMENT

About 80% of diseases treated in outpatient health care are chronic. Although much of the treatment is remarkably efficient as a result of medical research, its quality is often far from satisfactory. Many patients do not comply with instructions; fewer than 50% follow their treatment correctly. Patients are often inadequately informed about their condition, and few have been helped to manage or take responsibility for their treatment (124). Although most physicians are highly competent in diagnosis and treatment, too few educate their patients to manage their condition. There may be several reasons for failing to educate patients, such as too little time or lack of awareness of the need to do so. One reason is that the initial training of most HCPs, especially medical care providers, is based principally on diagnosis and selection of a therapeutic regimen.

One of the first reports on patient education was published in the New England Journal of Medicine in 1972 (127). A patient education program, described and managed by Miller and Goldstein 40 years ago in a Los Angeles county hospital, reduced the hospital stay in diabetic patients from 5.4 to 1.7 days/year/patient. This statistically shortened period was the same as that for nondiabetic hospital patients (1.2 days/year/patient). The incidence of diabetes-related comas was reduced by two-thirds (127). For the first time in the history of medicine, patient education was shown to play an important therapeutic role on a large scale. Since then, numerous studies of the effects of patient education in multiple (mainly chronic) diseases have been published.

Concept of therapeutic patient education

Healthcare providers tend to talk to patients about their disease rather than train them in the daily management of their condition. Therapeutic patient education (TPE) is designed to teach patients the skills of self-managing and adapting treatment to their particular chronic disease, as well as coping processes and skills. It should also help to reduce the costs of long-
term care for patients and society. This type of patient education is essential to the efficient self-management and quality of care of all long-term diseases or conditions, although acutely ill patients should not be excluded from its benefits.

Therapeutic patient education is managed by HCPs trained in patient education. It is designed to enable a patient (or a group of patients and their families) to manage the treatment of their condition and to prevent avoidable complications, while maintaining or improving quality of life (Figure 4). Its principal purpose is to produce a therapeutic effect additional to that of all other interventions (pharmacological, physical therapy, etc.) (128).

![Figure 4: Goals of therapeutic patient education](image-url)
In a recent review, we analyzed the effects of TPE in chronic diseases (129). A total of 35 meta-analyses and review articles were initially selected according to specific MeSH terms in the field of the most prevalent chronic diseases, corresponding to 598 individual studies and approximately 61,000 patients (Table 1). We further analyzed 60% of the papers in detail (360 individual studies), evaluating the description of the educative interventions and the efficacy of TPE.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Type and number of analyzed articles</th>
<th>Number of studies</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>4 meta-analyses, 3 reviews</td>
<td>60</td>
<td>12,000</td>
</tr>
<tr>
<td>Asthma</td>
<td>3 meta-analyses, 1 review</td>
<td>30</td>
<td>4,000</td>
</tr>
<tr>
<td>COPD</td>
<td>3 meta-analyses, 2 reviews</td>
<td>80</td>
<td>5,000</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 meta-analyses</td>
<td>100</td>
<td>8,000</td>
</tr>
<tr>
<td>Cardiology</td>
<td>3 meta-analyses, 1 review</td>
<td>63</td>
<td>8,000</td>
</tr>
<tr>
<td>Obesity</td>
<td>1 meta-analysis, 6 reviews</td>
<td>71</td>
<td>8,000</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>1 meta-analysis</td>
<td>17</td>
<td>4,000</td>
</tr>
<tr>
<td>Oncology</td>
<td>4 meta-analyses</td>
<td>177</td>
<td>12,000</td>
</tr>
<tr>
<td>TOTAL</td>
<td>22 meta-analyses, 13 reviews</td>
<td>598</td>
<td>~ 61,000</td>
</tr>
</tbody>
</table>

**Table 1: Main chronic diseases and review articles analyzed** (adapted from Lagger G. et al. Patient education and counseling 79:283-6, 2010 (129))

*COPD – chronic obstructive pulmonary disease.
Most studies (64%) in the review reported improvement of patient outcomes due to the TPE. Only 30% of studies reported no effect of TPE, and 6% of the analyzed reviews and meta-analyses reported worsening of measured outcomes (Figure 5) (129).

![Figure 5: Effect of therapeutic patient education on health outcomes](adapted from Lagger G. et al. Patient education and counseling 79:283-6, 2010(129))

When the TPE was complex and structured, with very precise indicators and a control group without TPE, education was highly effective in all considered chronic diseases. This finding can be explained by the overall effect of the patient education, which improved the understandings and beliefs of the patient and allowed subsequent behavioral changes through cognitive-behavioral therapies.

The benefits of patient education are often underestimated. In most of the meta-analyses that we analyzed, the control group was not systematically well defined. It can be difficult to keep information from an eventual “control group”. Patients who have entered the medical system cannot be blinded to any information or learning process. In some meta-analyses, this bias is clearly mentioned: for example, “40% of the studies gave both the control and intervention groups an initial educational intervention that was not trivial”, and “because
our main effect, net glycemic change, is the difference between the amount of improvement in the intervention group and that of the control group”. The real benefit of the intervention may be difficult to detect when the “control” is getting aid beyond “standard care” (130).

In randomized, double‐blinded studies, the aim is to approach the ideal situation in which only a single parameter of the healing process differs between the intervention and control groups. In patient education, the paradigm of the process is different; one can hardly separate the treatment (e.g., drugs, surgery, physical activity, diet, etc.) from the education. It is really the complex interaction of these dimensions that is efficient: i.e., “patient education is an integrated process”. It would not be correct to state that a benefit for the patient could come, as an example, 40% from education and 60% from drugs. The patient learns, tries a medicine, experiments, and receives new information from his/her body (i.e., the perceptive dimension of learning). The global result for the patient’s health is a resulting combination of the drug and the educational process. Both are necessary, and the effect of each cannot be separated or numerically defined (129).
Therapeutic patient education for preventing diabetic foot ulceration

Multiple studies have reported the beneficial effects of patient education on health outcomes of patients with foot ulcers. Most lower extremity complications are preventable through different educational programs for patients and HCPs (48, 131-133). According to Assal et al., the education and training of patients decreased the incidence of diabetes-related LEAs by 82% overall (133). From 1979 to 1989, the rates of above-knee, below-knee, and toe amputations were reduced 12, 2, and 4 times, respectively, at the University Hospital of Geneva (Figure 6) (133).

![Decrease of Lower Extremity Amputations after Patient Education](image)

**Figure 6:** Impact of therapeutic patient education on lower extremity amputations in Geneva (adapted from Assal J-Ph. et al. Diabete Metab 19:491-5, 1993 (133))
This specific educational program for both patients and HCPs has been shown to be cost-saving. According to cited study, the direct cost of only 9 LEAs corresponded to the annual salary of an HCP team of 3 physicians, 5 nurses, 3 nursing aides, 1 dietician, and 1 secretary (133). Several other clinical and financial models have indicated that the implementation of prevention programs may have help reduce the number of morbid events (27, 134-136) and costs (137-139). Multidisciplinary clinical programs have reported a decrease in amputation, reamputation, ulceration, and related hospitalization, length of stay, and missed work days (140). In a hypothetical cohort of 10,000 people with diabetes, the total potential economic benefits of preventive strategies (education programs, multidisciplinary approach, and therapeutic footwear coverage) ranged from $2.0 to $3.0 million over 3 years in the USA, with the highest economic benefit resulting from educational interventions (139).

The cost-effectiveness of preventing foot ulcers and amputations and the future costs of these complications were evaluated in a simulation model (138), which incorporated patient education, foot care, and footwear interventions. The results showed that providing all of the diabetic patients at risk for foot ulcers and amputations with optimal prevention would be a highly cost-effective or even cost-saving strategy. Patient education has been shown to reduce the incidence of ulceration and amputation (141). In a prospective randomized study, a 1-hour educational class resulted in a 67% reduction in the rates of ulceration and amputation. This class included a simple list of patient instructions (132). In addition to improving patient knowledge, a diabetic patient educational program may improve patient satisfaction (142).

Malone et al. (132) found that the amputation and ulceration rates were 3 times lower in the group with education compared to the control (no education) group, even with a relatively short follow-up (mean: 13.8 months). However, different results were found in a recent review of trials evaluating patient education in this field (29). Based on the analysis of 11 randomized controlled trials and systematic reviews published in the Cochrane database (143, 144), the authors concluded that there is insufficient robust evidence that limited
patient education is effective in achieving clinically relevant reductions in ulcer and amputation incidence. Reading this conclusion, one could speculate that limited patient education *per se* does not add any supplementary value to “classical” clinical care.

Two major concerns were noted in the Cochrane reviews (143, 144). First, the number of randomized controlled trials evaluating patient education in the field of diabetic foot disease was limited. An April 2012 search in the Ovid MEDLINE electronic database identified only 606 articles when using the following MESH headings: diabetic foot or foot care or diabetes mellitus and foot, combined with patient education or therapeutic patient education or educational program or information. Methodology and clinical heterogeneity of the studies were the major criticisms. Missing or inadequate randomization and blinding, selective follow-up, insufficient power and duration of follow-up, and high risk of bias were the main reasons that initially identified articles were excluded from the meta-analyses, systematic reviews, and review articles. Among these “excluded” articles were probably an undefined quantity of papers dealing with the efficacy and efficiency of patient education.

Second, when analyzing the reported methods of patient education, most studies did not describe the intervention sufficiently (e.g., when well-described, another researcher should be able to apply the same intervention in another study). For example, studies comparing the effects of using films and card games in addition to nonspecified “usual care” are not sufficiently precise to conclude that “patient education is of poor effectiveness and does not improve clinical outcomes”. Additionally, there are many anecdotal examples of what patient education means for some caregivers: e.g., use of videotapes, distribution of hand-outs, telephone calls, lectures, etc.

Finally, in most studies, the follow-up duration was rarely long-term. The order of weeks or months is not sufficiently long to evaluate the effects of any intervention that has the reduction of the recurrence rate of foot ulceration or LEA as its goal.
Educational programs for health care providers

The care of patients with diabetic foot or any other chronic disease depends on HCPs. The knowledge or evidence-based approach used by the HCP is not enough for an effective follow-up of these patients: the active involvement and motivation of the HCP are essential. If the physician, nurse, or other HCP is not motivated to help and “accompany” the patient in the long term, then the patient will not be motivated either.

For example, some general practitioners and even diabetologists do not examine the feet of their patients regularly. De Berardis et al. (145) observed that more than 50% of diabetic patients reported that they had not had their feet examined by their physician in the last 12 months. Over one-third of patients had never had their feet examined, even with the marked increase in the risk of foot complications due to the presence of neuropathy or PVD (145). Kirkman et al. found a low level of adherence by general practitioners to diabetes guidelines (146). One year after the development of local consensus guidelines, significant improvements were seen in foot exams (19% vs. 42%). These results demonstrate that HCPs are also responsible for some of the poor outcomes seen among patients with foot ulcers. After implementation of a program for HCPs, the overall amputation incidence among Alaska Native diabetic patients decreased from 7.6 to 2.7 per 1,000 (147).

We evaluated the impact of a specific educational program on theoretical knowledge in the field of “at-risk feet” in different HCPs (doctors, nurses, nursing aides, physiotherapists, occupational therapists, speech-language therapists, and psychologists) in a long-term care facility (26). The HCPs attended a structured educational program during a 1-year period based on a specifically developed consultation. The educational program consisted of a multidisciplinary biweekly consultation, managed by a specialist and attended by different HCPs in charge of the patient. An average of 5 patients was present at each consultation conducted in a consultation room. Presence of a foot ulcer and lower limb neuropathy were the criteria for patient selection who attended the consultation.
During each visit that lasted 45 minutes per patient, doctors, nurses, nursing aides, and other HCPs (physiotherapists, occupational therapists, speech-language therapists, and psychologists) actively participated in the discussion about the therapeutic and preventive strategies with both the physician in charge of the particular consultation and the relevant patient. Specifically developed teaching materials (e.g., posters, didactic consultation report forms) were used to facilitate the learning process.

During the 1-year period, each participating HCP accompanied at least 2 of his/her patients at the consultation. There was no staff turnover between baseline and 1 year. A questionnaire was developed and used to evaluate the (a) initial knowledge of the HCP in the field of “at-risk feet,” and (b) impact of the program on the knowledge of the HCP at 12 months after starting the program. Global improvement at 12 months was noted in all professional groups of HCPs, except doctors (Table 2) (26).

<table>
<thead>
<tr>
<th>Health Care Providers</th>
<th>Knowledge Score*</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>12-months after</td>
<td>p-value</td>
</tr>
<tr>
<td>Doctors</td>
<td>9.3 ± 1.2</td>
<td>9.6 ± 0.8</td>
<td>0.22</td>
</tr>
<tr>
<td>Nurses</td>
<td>7.5 ± 1.6</td>
<td>8.8 ± 1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nursing aides</td>
<td>6.8 ± 1.5</td>
<td>7.6 ± 1.9</td>
<td>0.005</td>
</tr>
<tr>
<td>Other HCP</td>
<td>6.8 ± 1.8</td>
<td>8.2 ± 1.7</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Table 2: Comparison of the knowledge score before and 12-months after starting the educational program in Geneva (from Pataky Z. et al. Int J Low Ext Wounds 6:69-75, 2007 (26))

HCP – Health care providers. *Presented results, as analyzed by Student t-test, are expressed as mean ± S.D.
Our study (26) suggests that an educational program based on a specific consultation is an effective modality to improve the theoretical knowledge and change the professional behavior of different HCPs, especially nurses and nursing aides. These two groups of HCPs in long-term care facilities should be more actively implicated in the screening and follow-up processes of foot lesions in patients with chronic neurological diseases and consecutive loss of pain sensation. The International Working Group on Diabetic Foot stated that, with the education of important HCPs and patients, close monitoring of the diabetic foot facilitating early risk identification followed by multidisciplinary treatment of at-risk feet could reduce LEA rates by as much as 85% worldwide (2).
Footwear

Inadequate footwear is the most common cause of minor foot trauma. Approximately 50% to 80% of patients with diabetes wear incorrectly fitted shoes (43, 148, 149), for myriad reasons that are beyond the scope of this work. Given that peripheral neuropathy leads to foot deformities, the footwear (particularly the insole) of such patients must be altered. However, it is not sufficient to have adequately fitted shoes; the shoes must also be worn. Daily practice shows that many patients do not wear their customized footwear on a regular basis; they instead walk barefoot or with only socks, etc. Moreover, the shoes must be inspected before every use. Shoe-related problems, such as their use and regular inspection by the patient, depend on how well the patient understands the importance of such behavior. This issue is a behavioral aspect of long-term and chronic diseases. It is also probably the most relevant determinant for reducing the incidence of foot ulcers.

The issue of foot deformities combined with reduced or absent pain sensation in diabetic patients underlies the importance of off-loading. Zones under prominent metatarsal heads, deformed toes, or other plantar areas are exposed to high plantar pressure. As already mentioned, 94% of diabetic ulcers occur under areas of increased plantar pressure (120). Reducing the plantar pressure under these foot regions is mandatory for the prevention and treatment of any plantar ulcer and could help to reduce the global burden of diabetic foot disease. This issue comes back to the vital importance for having protective, correctly adapted, and well-fitted shoes that are regularly worn and inspected by patients.

Foot off-loading techniques

Many pressure-relief devices are available for reducing high plantar pressure. Total contact casts (TCCs), which are considered to be the gold standard for pressure relief, and removable cast walkers are designed to relieve forefoot pressure (150). Compared with controls, TCCs can reduce the PPP of the forefoot by up to 87% (151, 152). However, a gap exists between
evidence-based guidelines and current practice. The proportion of patients using TCCs is extremely low, varying from 2% to 35% (153-155). Even when readily available, TCCs are often difficult to use and may restrict the patient’s ability to engage in typical daily activities.

Cast shoes and forefoot off-loading shoes may reduce PPP by 44% to 64% (152, 156). Various other therapeutic footwear options (e.g., rocker-bottom outsoles, custom-made insoles, shoe inserts) offer a forefoot PPP reduction of 16% to 52% compared to controls (152, 157-162). However, there is some evidence that rocker-bottom shoes could have a destabilizing effect on a perturbed stance, thereby increasing the potential for imbalance in healthy people (163). This potential disadvantage is especially important in the diabetic population, which is at a higher risk of falls (109, 164). Injectable liquid silicone has been proposed as an alternative to more familiar treatments for the prevention of foot ulcers (165, 166). However, no large studies are available to support the therapeutic value of silicone use in patients with diabetes.

Pressure relief is probably the single most important but also most problematic intervention in the care of foot ulcers (167). Even when healing is achieved, many diabetic patients develop recurrent ulcers, often at the same sites. To address these issues, diabetic patients with peripheral neuropathy of the lower limbs need to develop lasting changes in their walking habits. To reduce the incidence of foot ulcers and related long-term complications, diabetic patients should place their feet differently at each step to avoid applying high plantar pressures to the same areas.
BIOFEEDBACK

Biofeedback (Figure 7) is the process of becoming aware of various physiological functions by using instruments that provide information on the activity of those same systems, with the goal of being able to manipulate them at will (168). The technique of biofeedback is used in different fields of medicine. Processes that can be controlled include brainwaves, muscle tone, skin conductance, heart rate, headaches, migraines and pain perception, etc. (169, 170).

Figure 7: Optimal feedback control (from Scott S.H. Nat Rev Neurosci 5:532-46, 2004 (171))

Reduced or absent physiological feedback from peripheral sensory receptors of the feet is the origin of diabetes-related foot ulcers and wounds. When diabetes is complicated by peripheral neuropathy with the absence of pain sensation, even an initially small wound can transform into a deep ulcer that is unperceived by the patient. The subject continues to walk, which contributes to wound or ulcer worsening. The lack of an “alarm” signal from the body becomes harmful.
Searching for the gift that nobody wants

“Pain is a more terrible lord of mankind than even death itself,” Dr. Schweitzer (1931)

The above sentence was written by Dr. Schweitzer after his large experience of medical practice in the African jungle. Pain has been a major concern of humankind since its beginnings, and it has been the object of ubiquitous efforts to understand and control it. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (172).

The origin of the word “pain” is based on Greek word “poine” and the Latin “poena,” which suggest punishment and the consequences thereof. However, the sensation of pain contributes to one of the vital functions of the nervous system: to provide information about the occurrence or threat of injury. One could consider pain as an alarm for the brain of potential danger from outside or inside of the body. Without the negative experience of pain, operant conditioning would be impossible. For example, a person avoids a hot stove based on the prior experience that such behavior leads to a reinforcing consequence (i.e., escape from heat).

Biofeedback for gait modification

Studies have addressed the issue of changing the walking pattern of a subject (173-177). Biofeedback-based systems enable a subject to initiate new gait strategies by using visual or auditory information (178, 179). In patients with stroke or LEA, biofeedback has been used for gait rehabilitation and for reducing gait asymmetry (180-182). Recently, a wireless sensory feedback system was developed for real-time gait modification (183). With this device, visual, audible or vibrotactile sensory feedback is provided on the Android platform of a Smartphone. Preliminary findings (183) suggest that the device can influence the gait of the user. However, patient data are not available (only healthy participants were quantified).
Walker et al. assessed the ability of diabetic individuals to learn to use a lower extremity substitution device to cue gait pattern changes (179). In this case-control study, 30 patients with diabetes, peripheral neuropathy, and a history of foot ulceration were evaluated. The authors tested a “gait trainer” device that monitors each of the patient’s steps and alerts him/her by means of an auditory signal (beep) when the surface contact time reaches 80% of baseline. In this case, the remote sensors were embedded in the patient’s insole. Each sensor was in communication with the device via a thin flexible cable. The circuitry was mounted on a waist belt, and feedback was provided to the subject via an adapted earphone. The authors concluded that diabetic persons with neuropathy effectively used lower extremity sensory substitution (179). However, no confirmation studies with this “gait trainer” (published or accessible in April 2012) have been performed.

The efficacy of an in-shoe device for improving body weight-bearing was assessed in another study in patients admitted for rehabilitation (184). An audio signal was delivered each time a designed target of weight-bearing was reached. The method was reported to be very reliable, but was not confirmed by other studies.

Biofeedback for pressure relief

Limited literature exists in the field of biofeedback-induced gait pattern changes in diabetic patients with peripheral neuropathy. In healthy subjects, several methods and techniques have been proposed to reduce PPP by changing the walking strategy (176, 179, 185). Audiovisual biofeedback was used by Femery et al. in a healthy volunteer (175). An auditory signal warned the user when potentially harmful plantar pressures were being applied, and a visual signal specified the degree of pressure. The subject was able to modify his gait pattern in response to the biofeedback. The PPP threshold in that study was defined as 30% below the baseline value (175).
Another study showed the feasibility of partial and deliberate foot off-loading using a biofeedback device (186). Eight healthy subjects underwent tests in which auditory and visual signals informed them of an excessive, insufficient, or correct off-load. Using plantar pressure sensors integrated in customized insoles, the subjects performed tests on a treadmill. Of the 8 subjects, 5 significantly modified their gait patterns to reduce the plantar pressure by 5% (186). However, as in the above study, only healthy nondiabetic subjects were evaluated and no late retention data were reported (175, 186). More recently, walking pattern modifications and PPP reductions of up to 20% were demonstrated in a healthy volunteer when a baropodometric biofeedback device was used (174).

Mueller et al. showed a significant 27% decrease in forefoot PPP using the hip strategy when compared to the normal (ankle) strategy of walking (185). Seven patients were instructed to pull the leg forward from the hip to initiate swing rather than push off the ground with the foot. The long-term effects of this teaching of a new walking strategy were not determined. York et al. (187) taught the same new gait pattern as Mueller et al. (185) to diabetic patients with peripheral neuropathy. Unexpectedly, they did not observe a consistent reduction in plantar pressures across the foot. The feedback group received visual feedback regarding PPP after each practice trial. The no-feedback group received no feedback. The authors concluded that individuals with diabetic peripheral neuropathy were unable to use a "new" strategy gait pattern to reduce PPP values in the long term (1 week) (187).

To our knowledge, no study to date has evaluated foot off-loading by biofeedback in the at-risk foot zone of diabetic patients with peripheral neuropathy. Changing one’s gait, especially for an extended period of time, could be a challenge, particularly for patients with peripheral neuropathy.
PART TWO: OWN CONTRIBUTION

FROM BIOMECHANICS TO THERAPEUTIC PATIENT EDUCATION
DEVELOPMENT OF AN AMBULATORY FOOT PRESSURE DEVICE


We previously developed an ambulatory device (Figure 8 & 9) that measured foot pressure parameters, including the PPP, contact time, and plantar pressure integral (PPI), defined as the integral of the pressure over time. Based on the measured data, the device was able to generate an alarm signal that could alert the subject to modify his or her walking strategy, allowing off-loading of the at-risk foot. The device was developed in collaboration with the European Laboratory for Particle Physics (CERN) in Geneva and was presented as a technical note in the Journal of Biomechanics (178).

The device used force-sensing resistors (FSR 174®) produced by International Electronics & Engineering (IEE, Luxembourg). We coated the sensor with alimentary silicon (1-mm total thickness) for biocompatibility purposes. The sensors were applied directly to the skin of the at-risk area of the foot with adhesive
hypoallergenic tape. The FSR 174® sensors were connected to the device through coaxial SMC cables, and the patient carried the device attached to a belt (Figure 9).

**Pressure sensors of the Ambulatory Foot Pressure Device**

Repetitive infraliminar pressure has not been sufficiently considered and evaluated, primarily because most pressure measurement devices function with precision for only a few hours. The Ambulatory Foot Pressure Device (AFPD) uses FSR 174® sensors that are only sensitive to vertical forces (Figure 10).

![Figure 10: The FSR 174® sensor](image)

The electromechanical properties of the FSR sensors are influenced by the kind and thickness of the resistive substrate, the conductor geometry, and the conducting polymer formula. To prevent skin lesions, the sensor is coated with 1-mm-thick biocompatible alimentary silicon. The performance of the sensors decreases by only 5% after 10 million cycles (IEE, Luxembourg). The sensor has been calibrated by the Swiss Federal Office of Metrology. When no force is applied to its surfaces, its resistivity is 60 kΩ. The resistivity can vary as much as 1.3 kΩ with an application of 220 N. An FSR sensor with specific properties is characterized by its calibration curve of resistance (Ω) versus the vertical applied force (N).
(Figure 11). The reproducibility of the FSR sensor electrical response is excellent: 97.3% for a force of 50 N and 98.1% for a force of 220 N.

Figure 11: Calibration curve of the FSR 174® sensor\(^1\)
(from Report N° 133-2107 of the Swiss Federal Office of Metrology)
Gait characteristics as evaluated by the sensor

For research purposes, the term “gait” refers to the gait “seen” by the sensor applied in a determined area, i.e., the plantar zone at-risk for ulceration (Figure 12).

![Figure 12: Areas of a neuropathic foot at-risk for ulceration](from Pataky Z. et al. J Biomech 33:1135-8, 2000 (178))

For the sensor, a “gait” starts at time $t_0$ when the rising edge of the curve exceeds the threshold of 30 kPa, and stops at time $t_1$ when the falling edge of the curve goes under the threshold value. This threshold avoids electromagnetic noise and corresponds to a significant value of plantar pressure. The PPP is defined as the maximum value of pressure between $t_0$ and $t_1$. The plantar pressure integral (PPI) is defined by the integral of the pressure over time between $t_0$ and $t_1$. The duration of plantar pressure (DPP) is defined as $t_1 - t_0$ (Figure 13).
Figure 13: An example of acquisition by the diagnostic option of the AFPD (a diabetic patient with neuropathy and plantar ulcer) (from Pataky Z. et al. J Biomech 33:1135-8, 2000 (178))

The ambulatory device: in-shoe plantar pressure measurements and feedback alarm

The AFPD works with a frequency response of 96 Hz. The sensors are directly attached to the at-risk area under investigation by adhesive hypoallergenic tape. The FSR sensors are connected to the AFPD through coaxial SMC cables (Ø1.8 mm). The patient carries the AFPD attached to a belt (Figure 9). The AFPD amplifies the signals delivered by the sensors and sends the amplified signals to a PC through 2 LEMO cables. Data are stored on a PC, forming a databank. Plantar pressure parameters (PPP, PPI, and DPP) are computed by LabView®
(Graphical Programming for Instrumentation, version 3.1.1, National Instruments, Austin, TX).

The AFPD is also a long-term monitoring device that works in an ambulatory mode and allows the performance of daily activities. The device is equipped with a sound alarm signal which is triggered when the local pressure exceeds a determined threshold, the Critical Risk Pressure (CRP).

A gait whose PPP is greater than the CRP is called an "Overlimit Gait" (OG). Each channel has its own CRP which is determined and adjusted by the physician according to each patient. The CRP can be regulated at minus 20, 40 or 60% of PPP for a given patient. Furthermore, a switch allows the activation or deactivation of the warning signal.

The AFPD contains a 2 x 2kB FIFO (First-In-First-Out) memory to store both the PPP as well as the DPP values at each step which is over the CRP. In addition, the total number of gaits (TG) and the number of OG are also stored. As this system is stand-alone, it is completely mobile and does not prevent the patient from performing his or her daily activities. This mode is for in-shoe pressure measurement and rehabilitation. The ambulatory portable AFPD allows for eight days of recording, or up to 60,000 gait cycles. After this period, it is necessary to download the data to the computer.
The main characteristics of the AFPD are described in Table 3.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions</td>
<td>15.5 cm x 9.5 cm x 3.2 cm</td>
</tr>
<tr>
<td>Maximum Channels</td>
<td>2</td>
</tr>
<tr>
<td>Data Memory</td>
<td>2 x 2 kB</td>
</tr>
<tr>
<td>Sampling Rate</td>
<td>96 Hz</td>
</tr>
<tr>
<td>Maximum Recording Time</td>
<td>8 days</td>
</tr>
<tr>
<td>Resolution</td>
<td>7 bits</td>
</tr>
<tr>
<td>Weight</td>
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</tr>
<tr>
<td>Power Draw</td>
<td>12 mA</td>
</tr>
<tr>
<td>Power</td>
<td>4 x 1.5 V LR 6 batteries</td>
</tr>
</tbody>
</table>

**Table 3: Main characteristics of the Ambulatory Foot Pressure Device** (from Pataky Z. et al. J Biomech 33:1135-8, 2000 (178))

The system error is low as measured by a coefficient of variation which ranges from 2.4% to 5.0% under the metatarsal heads (Table 4).

<table>
<thead>
<tr>
<th></th>
<th>peak Plantar Pressure</th>
<th>Duration of Plantar Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st MTS</td>
<td>3rd MTS</td>
</tr>
<tr>
<td>Mean</td>
<td>52.4</td>
<td>65.9</td>
</tr>
<tr>
<td>S.D.</td>
<td>1.2</td>
<td>1.9</td>
</tr>
<tr>
<td>C.V.</td>
<td>0.024</td>
<td>0.030</td>
</tr>
</tbody>
</table>

**Table 4: Plantar Pressure Distribution of the test (non-diabetic) subject during walking**
(from Pataky Z. et al. J Biomech 33:1135-8, 2000 (178))
S.D.-Standard Deviation, C.V.-Coefficient of Variation
The mean values of PPP are expressed in kilopascals (kPa) and that of DPP in miliseconds (ms)
Acquisition system

To store the data, we used a PC equipped with a multifunction acquisition board (DaqCard-1200). The board contains 50 pins, such as digital I/O, analog I/O, and power supply. In the diagnostic mode, analog inputs are used, and the ribbon cable PR50-50F is connected to a simple electronic interface board for receiving analog signals delivered through LEMO cables to the electronic acquisition board. In the ambulatory mode, digital input/output is used, and the ribbon cable PR50-50F is directly connected to the AFPD.

Acquisition and analysis software

Data monitored by the AFPD are computed by LabView®, which allows us to produce 2 main programs: PODO and PODOSTAT. The PODO program is for acquisition and is compatible with the diagnostic and ambulatory modes. In the diagnostic mode, it stores data in a diagnostic file containing pressure curves. In ambulatory mode, the data is stored in an ambulatory file containing the total number of gaits and the number of overlimit gaits, as well as PPP and DPP. All files contain general medical and podiatry data.

The PODOSTAT program uses the diagnostic and ambulatory files as input. One option of PODOSTAT allows the user to analyze an ambulatory file in detail. Because all of the ambulatory files describe several “gaits”, the means of PPP, PPI, and DPP are computed. Another option of PODOSTAT allows the user to deal only with mean values of the plantar pressure parameters. The computation is made for all diagnostic files; therefore, it can encompass all of the patients. It allows global analyses, with a direct path to statistical software for analyses.

Illustrative case report

A 65-year-old woman, weighing 75 kg with body mass index 28.2 kg/m², had been a noninsulin-dependent diabetic for 13 years. She had known diabetic neuropathy and
presented with an ulcer under the first metatarsal head of the right foot. At the time of examination no deformities or callosities were noted. Figure 13 shows plantar pressure curves under the 1st and 5th metatarsal heads of the right foot. The mean plantar pressure is considerably higher under the first metatarsal head, at the site of the ulcer (450 kPa vs 200 kPa). The example acquisition on Figure 13 was made by the diagnostic mode of the AFPD and is a "zoom-in" on one of 50 measured steps.

To diminish the local pressure at the ulcer site, we chose to reduce the planar pressure by forty percent, and to trigger an acoustic alarm when the local pressure at each step exceeds this CRP. After a period of two weeks, the ulcer had been reevaluated and a significant clinical improvement and plantar ulcer diminishing from 14 mm to 5 mm had been noted. The mean PPP had been reduced to 200 kPa.

Our AFPD is a new device, specifically because it has an alarm feed-back device to provide a compensatory mechanism for the loss of pain sensation. It has a diagnostic value to determine the true plantar pressure in different areas of the foot in at-risk patients with peripheral neuropathy and loss of protective pain sensation. More importantly, it has a preventive value due to the acoustic signal which could induce behavioral changes during walking and reduce plantar pressure to a safe level.

The AFPD was used in some clinical studies of the diabetic foot (79, 91, 178, 188). However, it only allows pressure measurements under a limited number of foot zones, and do not provide information on the general plantar pressure distribution. Therefore, pressure shifts to another at-risk area could not be evaluated. Furthermore, its practical use in everyday life is not user-friendly. Regardless, this device represents the first time that a “behavioral” approach has been used to reduce high plantar pressure in diabetic patients with neuropathy.
IMPACT OF HYPERKERATOSIS ON PLANTAR PRESSURE


Background: The importance of high PPP in the development of foot ulcer is well known. However, few studies have analyzed the real impact of callosities on plantar pressure and ulcer formation.

Methods: The plantar pressure in patients with diabetes mellitus was studied in three groups, of a total number of 33 type 2 diabetic patients, without neuropathy or peripheral vascular disease: subjects with callus (n = 10), subjects without callus (n = 10), and a separate group of patients with callus which was submitted to callus removal (n = 13). The plantar pressure parameters were measured by FSR 174R sensors and computer analyses were performed by LabView®.

Results: Both PPP and DPP are significantly higher in patients with callus (PPP: 314 ± 52 kPa vs 128 ± 16 kPa, p < 0.005; DPP: 621 ± 27 ms vs 505 ± 27 ms, p < 0.05). The intervention group before and after callus removal showed an identical trend. Callus removal has decreased the PPP by 58% (p < 0.001) and DPP has been decreased by 150 milliseconds by step (p < 0.05).

Conclusion: This study has shown the deleterious role of callus and assuming that an average person walks about 10,000 steps a day, a callus may cause 18,600 kg of excess plantar pressure per day. In addition, this study has proven the importance of early and regular removal of hyperkeratotic tissue. Even more aggressive removal could be recommended in patients with neuropathy and peripheral vascular disease.
Many studies have shown the importance of PPP in the development of a foot ulcer (e.g., (10, 189)). These studies mostly underline the role of the effects of motor neuropathy (foot deformities or limited joint mobility) and autonomic neuropathy on elevated plantar pressure (106, 117). However, few studies analyze the callosities as an important risk factor and their real danger and impact on plantar pressure and ulcer formation. Patients with diabetes mellitus frequently present callus or hyperkeratosis on the plantar aspect of the feet (77). The hyperkeratinisation may result in a breakdown of skin and tissue integrity. As already mentioned, this is common in neuropathic diabetic patients who, in the absence of pain, have no warning of impending tissue breakdown. For such patients, who are assessed as being at high risk, the removal of callus plays a crucial role in both prevention of foot ulceration and its treatment.

In this study, both PPP and DPP were significantly higher in patients with callus compared to patients without callus (Figure 14 and Figure 15). The intervention group before and after callus removal showed an identical trend. Callus removal decreased PPP by 58%, PPI by 61%, and DPP by 150 milliseconds in each step ($650 \pm 33$ ms vs. $500 \pm 53$ ms, $p < 0.05$, Figure 16) (79).

![Figure 14: Effects of callus on peak plantar pressure at each foot step](image1)

![Figure 15: Effects of callus on duration of plantar pressure at each foot step](image2)

(Figures from Pataky et al. Diabetes Metab 28:356-61,2002)
Our results highlight that hyperkeratosis not only serves to increase the plantar pressure but also increases the pressure duration at each step. Infraliminar forces are an important problem in terms of tissue breakdown in the callused area: although not strong enough for tissue breakdown, they become pathological by their repetition. This issue raises the question of whether these small changes could be quantified over time.

Our findings show an increased PPP at the callus level of 186 kPa (= 1.86 kg/cm²) per step. If we assume that an average person takes about 10,000 steps per day, then these values indicate an excess of 18,600 kg per day on the callused area. For the DPP, the difference of 116 milliseconds per step corresponds to 20 minutes of overtime pressure per day. Extrapolations reveal that a callus causes an excess of 567,000 kg and 10 hours of weight-bearing per month (79).
RELATIONSHIP BETWEEN PERIPHERAL VASCULAR DISEASE AND HIGH PLANTAR PRESSURES IN DIABETIC NEUROISCHEMIC PATIENTS


**Background:** It has been shown that high foot pressure in diabetic patients plays a crucial role in plantar ulcer development. The purpose of the study is to analyze the relationship between foot arterial pressures and plantar pressures in diabetic patients with both peripheral neuropathy and PVD.

**Methods:** We have evaluated the relationship between foot arterial pressures and plantar pressure parameters (PPP, DPP, PPI) in eleven diabetic patients with both peripheral neuropathy and PVD. Peripheral neuropathy was defined as a tuning fork score < 4/8 (measured at the great toe and internal malleolus; Tuning fork 128 Hz Rydel-Seiffer®), the absence of both patellar and ankle reflexes and with a temperature discrimination more than +5°C (Thermocross®). The PVD was evaluated by Doppler technique. PPP and DPP were measured by FSR 174® sensors under the 1st, 3rd and 5th metatarsal heads as well as under the heel and big toe of both feet. The PPI was defined by the integral of the pressure over the time.

**Results:** We have found significant relationship between plantar pressure parameters (PPP, DPP, and PPI) under the first metatarsal heads and Doppler arterial pressures of both tibial posterior and dorsalis pedis artery. However, there was no relationship between Doppler arterial pressures and plantar pressure parameters (PPP, DPP, PPI) under 3rd and 5th metatarsal heads or under both the heel and the big toe.
**Conclusion:** According to our results, the PVD could contribute to the elevation of plantar pressures and to the prolonged DPP at each step in diabetic patients with both peripheral neuropathy and PVD. In such patients, severe ischemia could lead to an increased risk of foot ulceration and consecutive lower extremity amputation.

PVD is an independent risk factor for foot ulcers (190). About two thirds of patients with chronic, non-healing plantar ulcers have arterial insufficiency as a major factor (191). PVD plays a major role in delaying wound healing and is a contributing factor to almost half of the amputations (52). Although decreased blood flow and diminished oxygen supply are well recognized, the impact and implications of PVD on plantar pressure have not been evaluated.

We observed significant relationships between all plantar pressure parameters (PPP, DPP, and PPI) measured under the 1\textsuperscript{st} metatarsal heads and Doppler pressures of the tibial posterior and dorsalis pedis arteries in the 11 diabetic neuroischemic patients (Figures 17-20). There was no relationship between plantar pressure parameters and arterial pressures at the 3\textsuperscript{rd} and 5\textsuperscript{th} metatarsal head levels or under the heel and big toe. No differences in plantar pressure parameters were found between the right and left feet.
Our findings suggest that the degree of PVD may serve as a predictive factor for high plantar pressure in terms of its peak values and the duration. Severe ischemia in diabetic neuropathic patients could substantially elevate plantar pressure and increase the risk of foot ulceration and LEA.
PLANTAR PRESSURE DISTRIBUTION IN TYPE 2 DIABETIC PATIENTS WITHOUT PERIPHERAL NEUROPATHY AND PERIPHERAL VASCULAR DISEASE


**Background:** The majority of previous studies evaluated mostly the role of established peripheral neuropathy or PVD as a major cause of plantar pressure abnormalities. Our aim was to evaluate the distribution of plantar pressure during level walking in patients with type 2 diabetes mellitus without any microvascular and macrovascular complications and to compare them to non-diabetic control subjects.

**Methods:** A group of 15 patients with type 2 diabetes mellitus without either peripheral neuropathy or PVD, as well as without both diabetic retinopathy and nephropathy was compared to a group of 15 non-diabetic subjects matched for age, sex, body weight, and height. The PPP and DPP were measured on big toe, 1\(^{st}\), 3\(^{rd}\) and 5\(^{th}\) metatarsal heads, and on the heel of both feet by FSR 174\(^{\circ}\) sensors. The static contact plantar surface was measured by method of Harris footprints.

**Results:** The diabetic group showed a significant increase in PPP at the level of the big toe (Right foot: 205 ± 94 vs. 101 ± 39 kPa [mean ± SD], p = 0.01; Left foot: 165 ± 61 vs. 104 ± 43 kPa, p = 0.04) and 5\(^{th}\) metatarsal head (Right foot: 160 ± 68 vs. 97 ± 32 kPa, p = 0.04; Left foot: 174 ± 65 vs. 91 ± 42 kPa, p = 0.02) with a significantly prolonged DPP at each step. Under the heel, the PPP was significantly lower in the diabetic group (Right foot: 187 ± 54 vs. 321 ± 91 kPa, p = 0.05; Left foot: 184 ± 63 vs. 298 ± 110 kPa, p = 0.05). No significant differences were noted under 1\(^{st}\) and 3\(^{rd}\) metatarsal heads. The contact plantar surface was
significantly reduced in diabetic group compared to control subjects (Right foot: 118.2 ± 10.8 vs. 141.5 ± 12.7 cm², p = 0.04; Left foot: 127.5 ± 8.7 vs. 140.0 ± 11.1 cm², p = 0.05).

Conclusions: We have observed an anterior displacement of weight-bearing during a level walking as well as a reduced static contact plantar surface in diabetic patients without evidence of any complications compared to the non-diabetic control group. This could be a premature sign of peripheral neuropathy, which is not evaluated on clinical examination or quantitative sensory testing used in clinics.

In the present study, we have evaluated and quantified the plantar pressure distribution in type 2 diabetic patients without any micro and macrovascular complications and six years after the onset of diabetes mellitus. We have shown significantly increased PPP under the big toe and 5th metatarsal head; whereas the PPP on heel was significantly lower than in control non-diabetic subjects. These data are similar on both feet. In addition, we have found a prolonged DPP at same areas (big toes and 5th metatarsal heads) at each step. Therefore, an anterior displacement of weight-bearing can be observed in diabetic patients, even in early stage of diabetes, without any clinical evidence of peripheral neuropathy (Figure 21).

Figure 21: Plantar pressure distribution during normal walking in diabetic patients without complications (DM) and in nondiabetic control subjects (C) (adapted from Pataky et al. Diabet Med 22:762-7, 2005 (188))
It has been well documented that neuropathy could be anterior to diabetes discovery (72, 192). Boulton et al. reported reduced toe-loading in early diabetic neuropathy. However, the results were based on a global assessment of the whole area under all toes (193). Our results showing increased plantar pressure and DPP under the big toe are based on foot pressure evaluation under the hallux and in type 2 diabetic patients. The absence of plantar pressure evaluation under other toes could explain the differences in results. Moreover, the Boulton’s study (193) included patients with both type 1 and type 2 diabetes.

The tendency to plantar pressure displacement has been recently seen also by Caselli et al. (194). They have shown an increased both forefoot and rearfoot PPP in diabetic patients with peripheral neuropathy. They have suggested an imbalance in pressure distribution in severe neuropathy (increased forefoot-to-rearfoot plantar pressure ratio) (194). However, the cited study has not evaluated the plantar pressure in a control group of non-diabetic subjects.

The mechanisms by which the peripheral diabetic neuropathy is involved in plantar pressure elevation are well described (123). One of these mechanisms is the lack of proprioreception with an imbalance between the long flexors and extensors of the toes, which, in its advanced form, give rise to the claw toes and prominent metatarsal heads (10). Clawing of the toes is accompanied by anterior displacement of the submetatarsal head fat pads (102). These structural changes could lead to increased supinatory moments in the neuropathic feet with an increased pressure under 4th and 5th metatarsal heads (195). Those abnormalities in plantar pressure may occur before clinical evident peripheral neuropathy.

Our results showing the plantar pressure abnormalities in diabetic patients without complications confirm and put in concrete form this observation, thus abnormalities appear before loss of vibratory and temperature discrimination (in clinical examination and quantitative sensory testing) as an early sign of diabetic neuropathy.
It is of interest to observe that there is a relationship between TDT and both PPP values under the $3^{\text{rd}}$ metatarsal head and DPP under the big toes. Nevertheless, the values of TDT are not pathologically altered. The TDT has been described as a sensitive method of small nerve fibers evaluation (196). Because of this relationship between TDT and both PPP and DPP (even only at 2 different levels) in diabetic patients in the present study, we hypothesize that this could be due to an early stage of small fibers pathology and which could not be detected in clinical examination and quantitative sensory testing. No correlation between vibration perception threshold (VPT) and plantar pressure parameters was found. It has been seen that the defect of peripheral thermal sensation may occur independently of vibration perception (196).

For the first time, by measuring the contact plantar surface in diabetic patients in the early stage of the disease, a significant difference between the diabetic and the control group has been seen. This could partially explain the differences in plantar pressure between two investigated groups. We observed that the reduced plantar surface in diabetic patients is correlated with the prolonged DPP under the big toe ($p < 0.05$) and $5^{\text{th}}$ metatarsal head ($p < 0.001$). In other words, more the plantar surface is reduced, more the foot-floor contact is prolonged at each step. This could be an important contributing factor to ulceration in the neuropathic or neuroischemic foot where the contact plantar surface could be even more reduced because of underlined neurological or vascular pathology. The reduced contact plantar surface in our diabetic group, even in the early stage of diabetes mellitus, may be linked with other factors involved in increased plantar pressure. These could be the structural changes of the sole, especially the plantar soft tissue thickness. Edmonds et al. has reported that the plantar soft tissue thickness (measured by ultrasound scanning) is reduced in the neuroischemic foot compared with the neuropathic foot (92). Several authors have reported that plantar soft tissue thickness has been shown to be the strongest individual predictor of PPP (197-199). Moreover, changes in plantar fascia and joint mobility have been reported in diabetic patients, even in the absence of peripheral neuropathy. D’Ambrogi et al.
(200) concluded that such patients have a different pattern of plantar pressure distribution and that the plantar fascia alterations in the absence of neuropathy may be critical in the onset of the mechanical stress leading to the plantar pressure elevation (201, 202). This could also partially explain the correlation between the contact plantar surface and PP duration we have observed.

In conclusion, it has been previously seen that there is a tendency to increased plantar pressure under the forefoot in diabetic patients with neuropathy (194). This could explain that, in such patients, the area under metatarsal heads is the most frequently affected part of the sole by plantar ulcers. On the other hand, our results show the same tendency of the anterior displacement of weight-bearing in diabetic patients without any complications and after relatively short duration of diabetes. However, these patients have sufficient protective pain sensation to safeguard the feet from repetitive trauma that continues in the unprotected and insensitive neuropathic foot. It must be the combination of high plantar pressure and insensitivity that may lead to foot ulceration in the diabetic neuropathic or neuroischemic foot. Another additional risk factor in such patients could be the prolonged DPP, which participates to soft tissue traumatism at each step.

We conclude that the plantar pressure elevation together with the prolonged duration of the foot-floor contact time, even in the absence of sensory loss, may be a premature sign of neuropathy. This should alert clinicians and other health care professionals to the fact that a regular foot check-up as well as adequate footwear may be important even in diabetic patients without evident peripheral neuropathy. We suggest that such patients, in the presence of anterior foot pressure shift, could develop callus under the forefoot more easily, which in turn, could itself importantly increase the plantar pressure (79, 203, 204). Thus, a vicious cycle is therefore established.

The increased plantar pressure as well as the anterior displacement of weight-bearing in type 2 diabetic patients without evidence of any micro and macrovascular complications in
the present study might rise the hypothesis of an early process which could be a result of two factors: 1. Early peripheral neuropathy not detected on clinical evaluation and quantitative sensory testing, and 2. Plantar soft tissue thickness as well as plantar fascia abnormalities. However, the study limitation is the sample size, and additional studies on both plantar soft tissue and plantar fascia structures in early diabetes are needed to confirm our results.
BIOFEEDBACK-BASED TRAINING PROTOCOL

A limited number of clinical studies have evaluated the use of biofeedback for foot off-loading (174, 175, 178, 179, 186). As mentioned in the section Biofeedback for pressure relief (page 48), with the exception of 2 studies (185, 187), trials were mostly performed in healthy nondiabetic subjects or are case reports. Mueller et al. (185) and York et al. (187) showed contradictory results in diabetic patients with peripheral neuropathy when patients were instructed to pull the leg forward from the hip to initiate swing rather than push off the ground with the foot. Whereas Mueller et al. (185) found a significant decrease in forefoot PPP, York et al. observed that individuals with diabetic peripheral neuropathy were unable to use a "new" gait pattern strategy to reduce PPP in the long term (1 week) (187).

Here, we describe 2 training protocols that we developed for foot off-loading, based on biofeedback in 2 clinical situations:

1. Orthopedic patients requiring partial weight bearing, and
2. Diabetic patients with peripheral neuropathy and increased plantar pressure.
DEVELOPMENT OF A BIOFEEDBACK TRAINING PROTOCOL FOR FOOT OFF-LOADING IN PATIENTS WITH PARTIAL WEIGHT BEARING


**Background:** Partial weight bearing (PWB) is commonly instructed during the rehabilitation of patients with fractures, osteotomies, amputations, or arthroplasties of the lower extremity. Frequently, patients load the lower extremity of the affected side with the prescribed PWB on a bathroom scale in order to adjust to it. Our aim was to evaluate a new biofeedback training method based on visual delivery of information in patients after total hip arthroplasty (THA).

**Methods:** We conducted an intervention study with pre-post design in 11 patients (age 56.1±9.0 years), shortly after THA. The PEDAR® mobile system has been used for biofeedback training with the predefined PWB threshold of 20 kg. After the learning period, four retention tests, consisting of three successive walking cycles without feedback, were recorded for each patient: (1) acquisition test, (2) early retention test (after 30 minutes), (3) the day after, and (4) after 2 days. As main outcome we measured the pressure error and the maximum pressure force at each step before and after biofeedback training.

**Results:** A significant difference of pressure errors between the beginning and the end of the learning period has been measured (42.5 ± 22.5 N vs 3.7 ± 11.4 N; p<0.001). However, there was no difference between the beginning of the learning period and different retention tests (after 30 minutes, after 1 day, and after 2 days).
In term of maximal pressure force, there was a difference between the beginning and the end of learning (251 N vs 195 N; p<0.05). The retention tests do not showed significant differences as compared to the baseline values.

**Conclusions:** THA patients were able to use the defined PWB during a short period of time and shortly after stopping the training, both the pressure errors and the maximal pressure force attended the values before training. These results confirm the difficulties to achieve PWB in patients after THA.

For patients with a THA, it is important to restrict the activation of the hip abductors to avoid nonunion of the trochanters fragment, which may lead to functional disability (205). Although the relationship between the load under the foot and the load at the hip is complex, the conventional therapy is to restrict weight bearing.

The maximum amount of weight bearing or target load is prescribed by the treating surgeon and given in kilogram load or percentage body weight. The purpose is to reduce mechanical irritations during the postoperative healing phase, when aseptic loosening of the prosthesis could occur and endanger the long-term healing process (206). Frequently, patients load the lower extremity of the affected side with the prescribed PWB on a bathroom scale to adjust to it (207). Most patients, however, vastly exceed the limits set by the surgeon (mean, 225% (207) or 217% (208) of the prescription). Evidence suggests several reasons for overloading, one being that adjustment to the prescribed PWB using a bathroom scale does not reflect the dynamics of walking. Furthermore, a lack of upper body and arm strength could result in a patient being unable to adhere to the prescribed load (207, 208).

Other proposed procedures, such as extensive training in how to use a bathroom scale for loading, along with concurrent auditory feedback training, are not effective in reducing the produced ground reaction force (209, 210). Video-based instructions (211) and terminal augmented feedback training (212) can positively affect motor learning. Krause et al.
showed that training procedures containing didactic designed video instructions and terminal augmented verbal feedback concerning the deviation from the prescribed load appear to be helpful when the alignment to a prescribed partial load has to be learned (213). However, the cited study investigated healthy uninjured subjects only.

In 2009, we evaluated the effectiveness of a biofeedback method based on information about foot pressure intensity (214). Visual biofeedback was delivered as the basis for training to achieve foot off-loading in patients after THA. The biofeedback training protocol was developed in collaboration with the Faculty of Psychology and Educational Sciences of the University of Geneva (214) and will be detailed in the section Biofeedback-based learning protocol: practical considerations (page 81).

Eleven patients (9 males; mean age: 56.1 ± 9.0 years, range: 44–69 years; mean body weight: 79.5 ± 10.3 kg, range: 64–94 kg; mean height: 1.73 ± 0.07 m, range: 1.60–1.85 m) after THA who fulfilled the study entry criteria were recruited. Criteria for entry into the study were: ambulant patient suffering from coxarthrosis and admitted for THA, without history of type 1 or 2 DM, age ≤ 70 years old, and absence of both peripheral neuropathy and foot ulceration. Peripheral neuropathy was defined as a vibration perception threshold (measured at the great toe and internal malleolus) of less than or equal to 4 (128 Hz tuning fork, Rydel-Seiffer® (215)) and the absence of both patellar and ankle reflexes on clinical examination. Patients with memory impairments (Mini mental state examination < 24 (216)), history of rheumatoid arthritis, congenital defects, and foot deformities (e.g., Charcot deformity, prominent metatarsal heads, pes cavus, clawing of the toes, hallux valgus, and hallux rigidus) were excluded from the study.

Training was done in an isolated, calm, quiet place. It was started on the first day that the patient was able to stay in an upright position and leave the bed (1 or 2 postoperative days). The physiotherapist initially used a bathroom scale for security reasons (only 1 time) to avoid high foot loading (defined as a threshold of 20 kg). The patient produced some walking
strides, which were learned on parallel bars under the supervision of the physiotherapist, and was equipped with the PEDAR® system. The patient was instructed concerning the training that she/he would undergo to control foot off-loading. Based on the maximum weight allowed by the orthopedic surgeon, PWB was defined as 20 kg ± 5 kg (vertical ground reaction force). Feedback information was provided in the format illustrated in Figure 22. The upper red horizontal line represents the upper limit (i.e., weight bearing of 25 kg).

![Graph](image)

**Figure 22:** Example of biofeedback provided after each walking sequence and limits of security (horizontal lines).
Red horizontal line – 25 kg limit of security not to be exceeded. Total force (N) produced by the foot on the sensors as a function of normalized stride time.
Green curve – n\(^{th}\) stride (adapted from Pataky et al. Arch Phys Med Rehabil 90:1435-8, 2009)

The next day, the patient learned to walk on crutches under the physiotherapist’s supervision. We began sequences of learning to walk on the crutches (10 steps). After each sequence, the participant provided a subjective estimate of his/her performance and objective feedback (Figure 22) was provided by the PEDAR® system. This strategy of self-estimation of the patient’s own performance according to a given criteria, followed by
objective feedback (known as knowledge of results), is a very efficient strategy for sensorimotor learning (217). The patient was considered to have learned when 3 consecutive walking cycles of 10 steps were achieved with at least 70% of all steps being within ±5 kg of the 20 kg limit.

After the learning period, 4 retention tests of 3 successive walking cycles without feedback were recorded for each patient: (1) acquisition test (directly after practice), (2) early retention test (after 30 minutes), (3) after 1 day, and (4) after 2 days. As a primary outcome, for each walking cycle, we first measured the median PPP. If this value was inside the limits of tolerance (±50 N), then we considered it as a nil pressure error. If the median PPP was higher or lower than the limits of tolerance (i.e., 250 or 150 N), then the pressure error was computed as the absolute difference between the measured value and the upper or lower limit of tolerance, respectively. The maximum pressure force produced during each step was also measured.

Pressure errors at the beginning (42.5 ± 22.5 N) and end (3.7 ± 11.4 N) of the learning period showed significant differences ($p < 0.001$, $F_{1,10} = 16.55$, $\eta^2 = 0.623$). However, there was no difference between the beginning of the learning period and different retention tests (after 30 min, 1 and 2 days). The vertical ground reaction force showed a difference between the beginning (251 N) and end (195 N) of learning ($p < 0.05$, $F_{1,10} = 4.99$, $\eta^2 = 0.330$) (Table 4). The retention tests did not show significant differences compared to the baseline values.
<table>
<thead>
<tr>
<th>Period of training</th>
<th>Vertical ground reaction force (N)</th>
<th>p-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beginning (baseline)</td>
<td>251 ± 35</td>
<td>—</td>
</tr>
<tr>
<td>End</td>
<td>195 ± 43</td>
<td>0.04</td>
</tr>
<tr>
<td>Retention tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition test</td>
<td>199 ± 39</td>
<td>0.47</td>
</tr>
<tr>
<td>After 30 min</td>
<td>233 ± 74</td>
<td>0.64</td>
</tr>
<tr>
<td>After 1 day</td>
<td>268 ± 63</td>
<td>0.11</td>
</tr>
<tr>
<td>After 2 days</td>
<td>263 ± 68</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Table 5: Vertical ground reaction forces at the beginning and the end of the training period, and at different retention tests (adapted from Pataky et al. Arch Phys Med Rehabil 90:1435-8, 2009)

We concluded that THA patients were able to use the defined PWB during a short period of time. However, shortly after patients stopped the training, both the pressure errors and the maximal pressure force matched the pretraining values. These results confirm the previously reported difficulties in achieving PWB among patients after THA.
DEVELOPMENT OF A BIOFEEDBACK TRAINING PROTOCOL FOR FOOT OFF-LOADING IN DIABETIC PATIENTS WITH PERIPHERAL NEUROPATHY


**Background:** The reduction of high PPP in diabetic patients with peripheral neuropathy is mandatory for prevention of foot ulcers and amputations. We used a new biofeedback-based method to reduce the plantar pressure at an at-risk area of foot in diabetic patients with peripheral neuropathy.

**Methods:** Thirteen diabetic patients (age 60.8 ± 12.3 years, body mass index 29.0 ± 5.0 kg/m²) with peripheral neuropathy of the lower limbs have been studied. Patients with memory impairment were excluded from the study. The portable in-shoe foot pressure measurement system (PEDAR®) has been used for foot off-loading training by biofeedback. The learning procedure consisted in sequences of walking (10 steps), each followed by a subjective estimation of performance and objective feedback. The goal was to achieve 3 consecutive walking cycles of 10 steps with a minimum of 7 steps inside the range of 40-80% of the baseline peak PP. The PPP was assessed during learning period and at retention tests.

**Results:** A significant difference of PPP was recorded between the beginning and the end of the learning period (when the target for plantar pressure was achieved) (262 ± 70 vs 191 ± 53 kPa; p=0.002). The statistically significant difference between the beginning of the learning and all retention tests persisted, even in the 10 days’ follow up.

**Conclusions:** The terminal augmented feedback training may positively affect motor learning in diabetic patients with peripheral neuropathy and could possibly lead to a suitable foot off-
loading. Additional research is needed to confirm the maintenance of off-loading on long term.

In that study, we evaluated whether diabetic patients with peripheral neuropathy and without foot ulcers are able to learn a new walking strategy and change their walking pattern by using a biofeedback-based learning technique. To this end, we developed a new training protocol utilizing a system different from the previously described device which we developed (178). The training protocol that we recently developed is based on terminally augmented visual biofeedback.
Biofeedback-based learning protocol: practical considerations

For the practical application of the biofeedback protocol, we used the PEDAR® system (Novel GmbH, Munich, Germany), one of the most commonly used systems for in-shoe pressure measurement. The PEDAR® system enables plantar pressure monitoring under the whole foot, which was not possible with our previously developed system (page 51). PEDAR® is a pressure distribution-measuring system for monitoring local loads between the foot and the shoe (Figure 23).

![Figure 23: The modifiable Pedar® output](Image)

This in-shoe mobile system measures the dynamic sole pressure distribution, using flexible and size-adaptable insoles. The insole continuously measures the PPP under the whole foot, permitting the user to monitor the plantar pressure distribution during walking and biofeedback training. Each insole contains 99 capacitive sensors, and the sampling rate is
modifiable. The system can function in a mobile capacity with its Bluetooth™ technology that is able to communicate with a Bluetooth™-compatible notebook. The repeatability and reliability of the system have been reported as excellent (218, 219).

For all subjects, the same investigator provides the learning instructions and training and obtains the plantar pressure measurements. The functioning of the PEDAR® system and the feedback information (graphical representation of plantar pressure on a computer screen (Figure 24) are explained to the patient first.

Before starting the training, each patient undergoes a preliminary learning phase to understand the biofeedback information provided by the PEDAR® system. Patients are asked to walk as naturally as possible with installed PEDAR® insoles in their shoes. During this preliminary learning, after each walking sequence, patients receive information regarding

![Figure 24: Example of the visual biofeedback (PEDAR®) output provided to the patient after each walking sequence during the training procedure (adapted from Pataky et al. Diabet Med 27:61-4, 2010)](image-url)
the biofeedback related to the last 10 steps, and the target plantar pressure to be achieved is re-explained, i.e., the plantar pressure is to be within the “safe zone” between the 2 horizontal red lines (Figure 24) for most steps and in 3 consecutive walking sequences of 10 steps. When necessary, additional explanations are given to the patient for better understanding of the relationship between the local pressure under the at-risk zone, the information provided by biofeedback, and the target pressure to be achieved.

Once the preliminary learning phase is terminated and patients understand the learning instructions (i.e., the biofeedback provided by PEDAR®), the learning phase can start. Biofeedback training consists of walking sequences (10 steps), each followed by a subjective estimation of performance and objective visual feedback (graphical representation of plantar pressure) via the PEDAR® system. Figure 24 shows an example of the biofeedback output provided to the patient at the end of each walking sequence of 10 steps during the training procedure.

Patients are then asked to try a new walking strategy, without any help or suggestion of the investigator, while walking as naturally as possible and until the PPP under the ulcerated zone is reduced to a safe level. At the end of each walking sequence of 10 steps, the patient is asked to give his/her subjective estimation of performance and to check the PC screen (Hewlet Packard, color LCD monitor 19") showing the graphics (Figure 24) corresponding to the plantar pressure under the ulcerated zone at each step of the walking sequence. When 70% of the steps (e.g., 7/10 steps) during 3 consecutive walking sequences have the PPP at the level of the at-risk zone within the range of 40% to 80% of the baseline PPP, then the patient is considered to have learned and adopted his/her new walking strategy. This relatively large range of plantar pressures (40-80%) as a target is comfortable for patients who may have lost protective pain sensation. Use of a more narrow range could make learning more difficult or even impossible.
Physical characteristics of the studied population are summarized in Table 6.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>N (Diabetes Type 1/Type 2)</td>
<td>13 (2/11)</td>
</tr>
<tr>
<td>Women / Men</td>
<td>7 / 6</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>60.8 ± 12.3</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>82.9 ± 14.1</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.69 ± 0.08</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>29.0 ± 5.0</td>
</tr>
<tr>
<td>Diabetes Mellitus (yrs)</td>
<td>16.0 ± 10.6</td>
</tr>
<tr>
<td>HbA₁c (%)</td>
<td>8.1 ± 1.6</td>
</tr>
<tr>
<td>Vibration Perception Threshold (Right/Left foot)</td>
<td>2.0 ± 1.2 / 2.0 ± 1.2</td>
</tr>
</tbody>
</table>


The at-risk area was located on the forefoot in all subjects. The mean number of completed trials for the learning period was 9.8 ± 3.5.

A significant difference of PPP between the beginning and the end of the learning period was recorded (262 ± 70 vs 191 ± 53 kPa; p=0.002). The statistically significant difference between the beginning of the learning and all retention tests persisted, even in the 10 days’ follow up (Table 7).
<table>
<thead>
<tr>
<th>Training period</th>
<th>Peak Plantar Pressure (kPa)</th>
<th>P-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beginning (baseline)</td>
<td>262 ± 70</td>
<td>—</td>
</tr>
<tr>
<td>End</td>
<td>191 ± 53</td>
<td>0.002</td>
</tr>
<tr>
<td>Retention tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition test</td>
<td>200 ± 44</td>
<td>0.007</td>
</tr>
<tr>
<td>After 30 min</td>
<td>205 ± 56</td>
<td>0.01</td>
</tr>
<tr>
<td>After 1 day</td>
<td>216 ± 45</td>
<td>0.04</td>
</tr>
<tr>
<td>After 5 days</td>
<td>209 ± 58</td>
<td>0.04</td>
</tr>
<tr>
<td>After 10 days</td>
<td>210 ± 51</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 7: The peak plantar pressures at the beginning and the end of training period, and at different retention tests (from Pataky et al. Diabet Med 27:61-4, 2010)

*As compared to baseline

We showed that foot off-loading under an at-risk area was achievable by learning with the biofeedback technique. After biofeedback training, patients reduced the PPP under a predetermined area of the at-risk foot during the learning period and maintained this “new” walking strategy at the 10-day follow-up visit. However, the patient was not followed-up beyond the 10-day time period; therefore, it is unclear for how long the achieved gait pattern will be applied by the patient.

In this article in the field of biofeedback applications in diabetic patients, we concluded that the decrease or loss of warning signals from the foot secondary to peripheral neuropathy does not prevent patients from achieving new gait patterns or walking habits or from subsequent foot off-loading (177). However, it was not known whether the new gait pattern after biofeedback intervention would induce the development of new “hot spots” with high plantar pressures under foot zones different from those before the intervention. The development of such new at-risk area(s) of the foot in a patient with peripheral neuropathy
could be potentially harmful and may contribute to new ulcer formation. Therefore, we designed another study to evaluate the plantar pressure distribution after biofeedback training.


**Background:** Plantar pressure reduction is mandatory for diabetic foot ulcer healing. Our aim was to evaluate the impact of a new walking strategy learned by biofeedback on plantar pressure distribution under both feet in patients with diabetic peripheral neuropathy.

**Methods:** Terminally augmented biofeedback has been used for foot off-loading training in 21 patients with diabetic peripheral neuropathy. The biofeedback technique was based on a subjective estimation of performance and objective visual feedback following walking sequences. The patient was considered to have learned a new walking strategy as soon as the PPP under the previously defined at-risk zone was within a range of 40–80% of baseline PPP, in 70% of the totality of steps and during 3 consecutive walking sequences. The PPP was measured by a portable in-shoe foot pressure measurement system (PEDAR*) at baseline (T0), directly after learning (T1) and at 10-day retention test (T2).

**Results:** The PPP under at-risk zones decreased significantly at T1 (165 ± 9 kPa, p<0.0001) and T2 (167 ± 11, p=0.001), as compared to T0 (242 ± 12 kPa) without any increase of the PPP elsewhere.

At the contra-lateral foot (not concerned by off-loading), the PPP was slightly higher under the lateral midfoot at T1 (68 ± 8 kPa, p=0.01) and T2 (65 ± 8 kPa, p=0.01), as compared to T0 (58 ± 6 kPa).
Conclusions: The foot off-loading by biofeedback lead to a safe and regular plantar pressure distribution without inducing any new “at-risk” area under both feet.

In a cohort of patients with diabetes different from our previously cited study (177), in addition to showing the efficacy of biofeedback on plantar pressure under the at-risk area (confirming our previous findings in a different cohort), we also showed that learning by biofeedback reduced the global plantar pressure to a safe level under the whole foot (Table 8) (220).
<table>
<thead>
<tr>
<th>Foot zone</th>
<th>At-risk foot</th>
<th>Contra-lateral foot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (T0)</td>
<td>End of learning (T1)</td>
</tr>
<tr>
<td>Zone 1 (Heel)</td>
<td>130 ± 6</td>
<td>121 ± 10</td>
</tr>
<tr>
<td>Zone 2 (Heel)</td>
<td>135 ± 7</td>
<td>134 ± 11</td>
</tr>
<tr>
<td>Zone 3 (Median Midfoot)</td>
<td>35 ± 3</td>
<td>30 ± 3*</td>
</tr>
<tr>
<td>Zone 4 (Lateral Midfoot)</td>
<td>54 ± 5</td>
<td>70 ± 6*</td>
</tr>
<tr>
<td>Zone 5 (1st MTS)</td>
<td>162 ± 11</td>
<td>134 ± 15*</td>
</tr>
<tr>
<td>Zone 6 (2nd-3rd MTS)</td>
<td>183 ± 9</td>
<td>158 ± 11†</td>
</tr>
<tr>
<td>Zone 7 (4th MTS)</td>
<td>130 ± 9</td>
<td>134 ± 12</td>
</tr>
<tr>
<td>Zone 8 (5th MTS)</td>
<td>62 ± 5</td>
<td>65 ± 7</td>
</tr>
<tr>
<td>Zone 9 (Great Toe)</td>
<td>145 ± 17</td>
<td>79 ± 10‡</td>
</tr>
<tr>
<td>Zone 10 (2nd-4th Toes)</td>
<td>78 ± 9</td>
<td>54 ± 6†</td>
</tr>
<tr>
<td>Zone 11 (5th Toe)</td>
<td>44 ± 7</td>
<td>27 ± 6‡</td>
</tr>
</tbody>
</table>

Table 8: Peak Plantar Pressure distribution under different foot zones after biofeedback learning, as compared to baseline. (from De Léon et al. Diabetes-Metab Res Rev, 2012, in press). Results are expressed as mean ± S.E. As compared to baseline (T0): * p<0.05; † p<0.01; ‡ p<0.001

The original aspect of the present study is the demonstration that after learning by biofeedback, the plantar pressure was regularly distributed under both at-risk and contra-lateral foot. Thus, the foot off-loading by biofeedback lead to a safe and regular plantar
pressure distribution without inducing any new “at-risk” area under both feet. When analyzing the pressure distribution, there was a significant decrease of PPP under the forefoot of the at-risk foot, while on the contra-lateral foot, the PPP was significantly increased under the lateral midfoot. This could suggest that patients achieve the foot off-loading by redistributing the plantar pressure homogenously from the at-risk area to the whole foot (i.e., concerned by off-loading) and by shifting the pressure on lateral side of the contra-lateral foot (not concerned by off-loading). This new walking pattern does not lead to increase of plantar pressure at any other areas of feet.

Existing off-loading devices (e.g., total contact casts, removable walkers, therapeutic footwear), when adequately used, are extremely effective for ulcer healing. On the other hand, the recurrence rates of neuropathic ulcers remain high (221-223) and, in the same patients, ulcers may occur frequently under the same area of the same foot (224). Cavanagh et al. suggested that there could be a need for continuous off-loading in these patients (225). Even if the existing off-loading devices are effective in acute phases, it seems not realistic to propose these tools for secondary prevention and for a long term period.

Owings et al. (224) measured in-shoe plantar pressures in a group of patients with diabetic neuropathy who had prior foot ulcers which had remained healed. After a median of 3 years since healing, many of these patients had extremely high pressures at prior ulcer sites. As measured by the same instrumentation as in our study, an in-shoe pressure goal of < 200 kPa has been proposed by the authors. Other studies have shown that in-shoe pressure can be systematically reduced to the 200 kPa range (226, 227). In our study, the mean in-shoe PPP under the at-risk area was 165 ± 9 kPa at the end of learning and remained stable in the 10-day retention test (167 ± 11 kPa), suggesting that the foot off-loading by a biofeedback approach could be a valuable method for a safe plantar pressure reduction.

To our knowledge, this is the first attempt to demonstrate that patients with diabetic peripheral neuropathy and loss of protective pain sensation are able to off-load the at-risk area of foot by biofeedback without developing any new “hot spot” potentially at-risk for
ulceration. The biofeedback technique, as used in the present study, could be an additional and valuable tool to the existing devices (e.g., therapeutic footwear and insoles) for treatment and prevention of diabetic foot ulcers on long term. When considering that the recurrence rates of neuropathic foot ulcers are high it seems reasonable to suggest new techniques or devices that may help these patients to modify their walking pattern which should persist on the long term.

It has been shown since many years that the majority of lower extremity complications are preventable through different educational programs for patients and health care providers (48, 131, 167). Experience has shown that patient education itself is not sufficient on long term. Multiple approaches combining education and new techniques based on instrumentation could be more effective in terms of primary and secondary prevention of lower extremity amputations.

Some limitations to this study should be discussed. First, the sample size is small. It should be mentioned, however, that the existing literature in the field of biofeedback used for foot off-loading is limited; studies mostly present results of healthy volunteers or in particularly small sample sizes. To our knowledge, no study evaluating the potential “side” effects of biofeedback in patients with insensate feet is available.

Second, we used the 128-Hz Rydel-Seiffer® tuning fork and not neurothesiometer for peripheral neuropathy testing. However, it has been shown that tuning fork reliably detect lower limb neuropathy in comparison with the neurothesiometer and that the tuning fork is a useful screening test for diabetic neuropathy (228).

Finally, the persistence of the new walking strategy induced by biofeedback learning should be confirmed on a longer follow-up period.
CONCLUSIONS

Diabetic foot ulcers and related complications, mainly in terms of LEAs, remain a major public health problem with a huge and irreversible impact on the quality of life of patients. Foot off-loading is mandatory for the primary and secondary prevention of amputations in these patients. Despite the enormous effort made in the last 20 years in the fields of diabetes and foot biomechanics, the incidence of LEAs remains very high. A gap exists between knowledge, available technologies, and evidence-based approaches on one side, and everyday practice in foot clinics and the remaining high incidence of amputations on the other.

Highly evidence-based and extremely efficient approaches exist to reduce the suffering of people with diabetes. Unfortunately, they are largely unused, not prescribed by physicians, or associated with poor patient adherence. Therapeutic patient education seems to improve patient outcomes; however, to date, data on the long-term efficacy of this patient-centered approach have been lacking. Experience has shown that physicians or other HCPs should not “skip” the relationship with the patient. Decision-making must be based on regular discussion with the most concerned people – suffering patients. The combination of TPE and existing or new techniques may be the future that could reverse the actual trend of foot complications in diabetes.

Biofeedback-based methods have proven their efficacy in different fields of medicine. Clinically useful applications have been developed and are used for foot off-loading in orthopedics and neurology. We have developed a learning protocol combining biofeedback generated by electronic insoles with an individualized and patient education-based approach. With this new technique, patients with diabetes are able to change their walking habits and gait pattern to reduce the high plantar pressure in at-risk areas of foot. This improvement was possible even in presence of peripheral neuropathy of the lower limb. For the first time, we showed that peripheral neuropathy may not be a barrier to changing...
walking habits present since the beginning of one’s life, even when the protective pain sensation under the feet is highly reduced or totally absent.

The biofeedback technique, as developed and used in our previously cited works, could be an additional and valuable tool to existing devices (e.g., therapeutic footwear and insoles) for the treatment and prevention of diabetic foot ulcers in the long term. Given the high recurrence rates of neuropathic foot ulcers, it seems reasonable to suggest new techniques or devices that may help these patients to modify their walking pattern in the long term.

It is well accepted that most of the lower extremity complications are preventable through different educational programs for patients and HCPs (48, 131-133). However, experience has shown that TPE itself may not be sufficient in the long term (29, 143). Multiple approaches combining TPE and new techniques based on instrumentation could be more effective in terms of the primary and secondary prevention of LEAs.

In our project, an electronic device is used to develop biofeedback for excess plantar pressure control during walking. The patient himself is involved in the complex process of modifying his/her walking behavior after the loss of pain sensation. To change walking habits, the patient must incorporate external feedback into his/her behavior by combining electronics and TPE. This process is a new step not only in the field of diabetic foot management, but also in a larger bio-psycho-social context. The main idea behind our project, i.e., identifying biofeedback that impacts the walking strategy and is closely linked with the consequences of the absence of pain sensation, is a new approach in medical and human sciences.
Ongoing projects and perspectives

To evaluate the effectiveness of the recently developed biofeedback-based training for plantar pressure reduction in patients with diabetes and peripheral neuropathy of the lower limb, it is necessary to study patients with an active plantar ulcer. To date, no study has evaluated the effects of biofeedback on foot plantar ulcer off-loading.

To this end, we designed a research protocol based on a randomized control trial of 72 diabetic patients (types 1 and 2) with peripheral neuropathy and with a newly diagnosed plantar ulcer. Patients with severe PVD and memory impairment will be excluded from the study. Patients receiving standard treatment \((n = 36)\) will be compared to patients receiving the biofeedback intervention in addition to standard treatment \((n = 36)\). All patients will be examined on a weekly basis during the treatment period of 3 months and on a monthly basis during the 18-month follow-up period.

The primary outcomes will be the clinical efficacy of this visual terminally augmented biofeedback training, specifically in terms of:

- Time to complete healing, and
- Percent reduction in ulcer surface area.

As secondary outcomes, the proportion of complete wound healing at 3 months and the recurrence rate at 18 months will be assessed in both groups. Plantar pressure parameters and gait parameters will be evaluated at baseline, at the end of the treatment period, and at 6, 12, and 18 months during the follow-up period.

To the best of our knowledge, no study has addressed foot off-loading by biofeedback training in diabetic patients with neuropathic foot ulcers. We previously developed and used a biofeedback-based training protocol in diabetic patients with neuropathy and no foot ulcers. Our project aims to evaluate the efficacy of such off-loading in diabetic patients with
plantar ulcers. This new approach, if clinically relevant in the long term, could be a valuable method for plantar ulcer treatment and LEA prevention in diabetic patients with peripheral neuropathy.
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List of annexes


