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DIABETIC FOOT SYNDROME

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Abstract
Diabetic foot syndrome is more and more actual, considering the rising number of people suffering from diabetes mellitus, a situation associated with the population demography. It is a late complication of this illness that significantly decreases the quality of the patient's life. Diabetic foot syndrome is a very serious health, social and economic problem, mainly because of the incidence, length and demands of the therapy, high risk of amputation and significant social and economy obligation for the society. According to the international consensus for the diabetic foot syndrome from the year 1999, the care for diabetic patients takes up 12–15% of healthcare system finances. Amputation due to diabetic gangrene form more than a half of non-traumatic amputations in the Czech Republic, unfortunately, the amputations count rises all the time.

Key words: *diabetic foot syndrome; amputation; ulceration; pathogenesis; prosthetics*

REVIEW

"... and diabetic mortification can be dry or wet..., a small and even bluish spot appears on the skin that doesn't hurt, possibly only a little, spreads to the sides and the surrounding, even to the depth, as a stone thrown into water. ... the middle part caves in, turns into an ulcer, covers with a stinking, ceruminous material. The necrosis continues to the tendons and bone, then the tissue disintegrates and it is necessary to perform an amputation. Otherwise, there is a risk of blood poisoning and death."

(Avicenna, 980–1037 in Canon)

INTRODUCTION

Diabetic foot syndrome definition

Diabetic foot syndrome is defined as an ulceration of affection of the deep tissues of the foot distally from the ankle, including the ankle. In addition to ulcerations, the patients suffer from gangrenes, osteomyelitis, Charcot's osteoarthropathy and infections of deep tissues (Jirkovská 2006a). The diabetic foot syndrome is from clinical view divided, according to the predominant pathogenetic factor, to neuropathic foot (45% of the cases), ischemic foot (25% of the cases) and neuroischemic foot – mixed (30% of the cases).

Neuropathic foot is warm, pink with significant venous filling in the instep area, the peripheral pulsations are easily palpable. The sensory and autonomous innervation, regulation of the capillary flow and flow through arteriovenous short-circuits is distorted, sweating is limited, the skin is dry with ragades. Ulcerations are localized in the areas of highest pressure (the pad of the toe, the area of the metatarsal heads and in the area of the heel), they are painful.

The ischemic foot and the neuroischemic foot is livid, calm, both claudications and resting pains may be present, but not necessarily due to simultaneous neuropathy presence.

Atherosclerosis of the lower extremity arteries is present, the most often from the popliteal artery.

The diabetic foot syndrome classification according to Wagner-Meggitt (Table 1) is a clinical classification based on assessment of the ulceration depth and the infection presence. It correlates well with the clinical severity, it is a method of amputation need estimation.

Table 1. The diabetic foot syndrome classification according to Wagner-Meggitt

Level	Lesion description
0	foot with a high risk of ulcerations
1	superficial ulceration
2	deep ulceration without an inflammation
3	deep ulceration, phlegmone, abscess, osteomyelitis
4	localized gangrene
5	gangrene of the whole foot

Diabetic foot syndrome incidence

The registered diabetics number in the Czech Republic rises from year to year, in the year 2010, 806,230 patients were treated due to diabetes. When comparing with the year 2000, the number was increased by 150 thousand. The number of patients treated only with diet amendments decreases, however, the number of the patients treated with medicaments rises. Chronic complications chronically appear in 27% of treated diabetic patients. In the year 2010, 45,118 patients were treated due to the diabetic foot, out of those 8,501 reached the amputation stage (Table 2).

Table 2. The diabetic foot syndrome incidence and the number of amputations

	2000	2005	2010
Diabetic patients number	654 164	739 305 (113%)	806 230 (123%)
Patients with the diabetic foot syndrome	37 764	38 090 (101%)	45 118 (119%)
Number of amputation	5 865	7 303 (124%)	8 501 (144%)

Source: ÚZIS (Institute for healhtcare information and statistics of the Czech Republic)

In the year 2010, 1.05% of all the diabetic patients in the Czech Republic had to undergo amputation (ÚZIS [Institute for healthcare information and statistics of the Czech Republic]).

The incidence of amputations under the knee level is 12–15times higher in diabetic patients, when compared with individuals without diabetes. Transmetatarsal amputations are 400times more common in diabetic patients. More than 60% of patients undergoes the amputation of the second foot within 4 years of losing the first extremity (Rušavý et al. 1998). Individual living alone, with insufficient education and individuals with low social and economy level have an increased risk of amputations. Other groups with high risks consist of patients with renal insufficiency, as the nitrous substance retention worsens wound healing; patients after a renal transplantation due to immunosuppressive therapy and patients with sight disorders (International working group for the diabetic foot syndrome 2000). Various studies repeatedly state that the pacients with high risks aren't provided with a podiagric preventive care of a sufficient level (Lavery et al. 2010).

Risk factors for ulcerations appearance

Hyperglycemia

Diabetic foot emergence reasons are multifactorial. The first place in the list holds the hyperglycemia, the connection between the hyperglycemia and the late complications emergence is proven. A short-term hyperglycemia influences microcirculation, decreases the immunity of the organism and the reologic blood characteristics, increases the oxidative stress, agregabitility and adhesivity of the platelets.

Diabetic microangiopathy – specific changes of arterioles, precapillaries and capillaries due to long-term hyperglycemia – is very serious. The thickened basal membrane with distorted permeability, resulting in decreased oxygen supply to the nutritive skin capillaries that can be even lower than 10%. At the same time, the total blood flow through the diabetic foot is increased, the endangered feet are warm, reddish, with widened venous system, can be even edematous. The edema worsens the skin hypoxia.

Atherosclerosis

Atherosclerosis is another very important factor. Ischemic illness of the lower extremities appears 2–4times more often in the diabetic patients than in the non-diabetic individuals. Typically, the crural and foot arteries are damaged, up to 80% of the changes on the arteries is distally of the popliteal artery. Another typical factor is the mediocalcinosis – calcification of the arterial media. 5–10% of diabetic patients suffer from this condition; it doesn't have to worsen the peripheral circulation. The vessel wall damaged by mediocalcinosis is difficult to compress, therefore peripheral pressure in Doppler method measurement are falsely too high. Quicker atherosclerotic changes in the diabetic patients are caused by risk factors accumulation (dyslipidemia, hypertension, hyperglycemia, hyperinsulinemia, glycation of the LDH-cholesterol and collagen, hypercoagulation condition and endothelial dysfunction).

Ischemic illness of the lower extremities is often without any clinical signs, claudication pain appears often in the ankle area and more distally, moreover, the claudication pain sensing may be modified by the neuropathy presence (Piťhová 2006).

Diabetic neuropathy

Diabetic neuropathy is the most serious factor of the diabetic foot development. Diabetic neuropathy is a diffuse, non-inflammatory distortion of the function and structure of peripheral motor, sensitive and vegetative nerves. It leads to slowing the stimuli conductivity through the nerve fiber.

The most common sign of the sensory neuropathy is the feeling of cold feet, hyperesthesia, paresthesia – burning, whip-like, stinging feet pain. On the other hand, the patients lose the ability to sense warm, cold and vibrations. As the diabetic patient doesn't feel the pain in his/her feet, he doesn't pay attention to them and he/she won't treat small injuries on time.

Motor neuropathy in a diabetic patients leads to an atrophy of small muscles of the foot, dysbalance of the flexors and extensors leading to stronger flexor action and chronic toes flexion, resulting in trigger fingers and the architecture of the foot changes. The pressure is overly transferred to the metatarsal and toe area, the gait biomechanics in general is distorted. Neuropathy leads to the loss of deep perception, loss of the tendon reflexes and intercostal muscles atrophy.

A joint movement limitation appears in up to 30% diabetics. It is caused by collagen glycation leading to skin and joint sheath thickening and rigidity, appears mainly in subtalar joints. It results in plantar pressure increase during walking. Hyperkeratosis formation in higher plantar pressure and autoimmune neuropathy can have the same effect as a foreign body and increase the plantar pressure even more. It culminates in Charcot's arthropathy development – it stands for very advanced foot bone structure deformities.

Autonomous neuropathy leads to sweating decrease or even to anhidrosis. Dry skin is more prone to injury and hyperkeratosis formation. Losing of tonus in sympatic nervous fibers of small vessels results in decreasing of peripheral vessel resistance and opening of arteriovenous short-cuts and further decrease of flow through the nutritive capillaries. The whole condition leads to tissue hypoxia (Piťhová 2008).

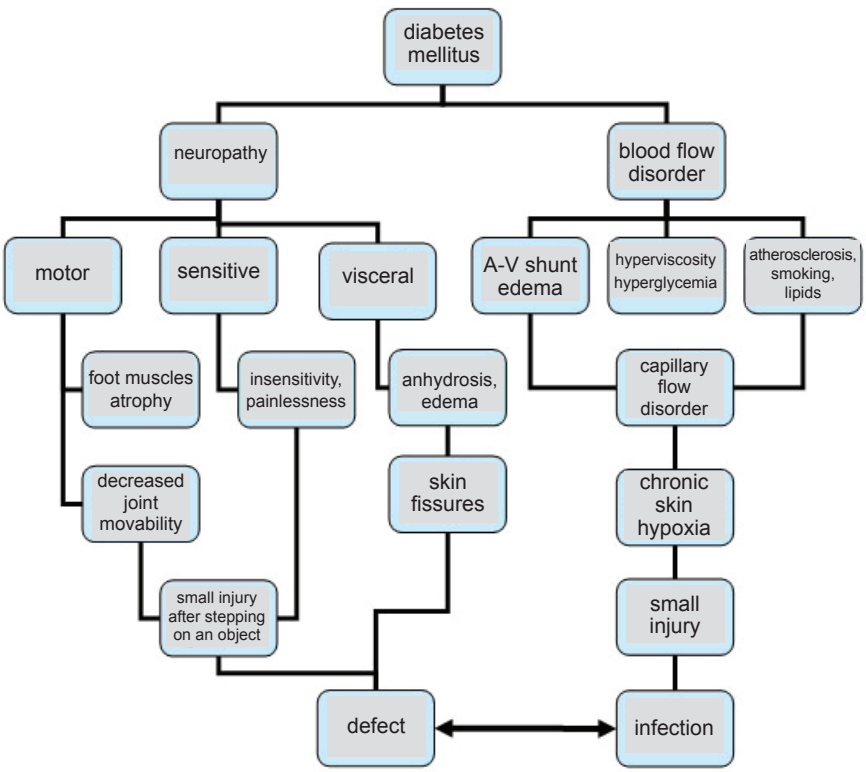
Charcot's osteoarthropathy can appear in up to 10% of patients with diabetic neuropathy and 16% of patients with neuropathic ulcerations. The highest risk is associated with the patients between 50 and 60 years of age with the diabetes duration for longer time than 10 years (Jirkovská 2003). It is a progressive destructive illness of foot bones and joints in the patients with a neuropathy. The exact pathogenetic mechanism isn't known.

The causes of diabetic defect emergence:

- chronic low pressure for many hours (when using improper shoes);
- direct injury (nail, a foreign body in the shoe);
- chronic slight pressure leading to a blister and then to an ulcus;
- scald, burns;
- radages, mycoses.

In addition to the above mentioned causes, some additional illnesses (hypertension, hyperlipidemia) and the life style of the patient – smoking – contribute to the pathogenesis.

An infection in the diabetic foot is defined as an invasion and multiplication of microorganisms in the tissue, tissue destruction and inflammatory response. The division to 1. no risk for the extremity; 2. risk for the extremity and 3. risk for the patient is really practical. Antibiotic therapy of the infection must always be supplemented with a complex care, relieve of pressure on the ulceration, surgery intervention (incisions, drainages, infected tissue removal via resection or amputation), débridement of necrotic tissue, vascular blood supply and metabolic compensation (Jirkovská 2006b). Infection in the diabetic foot is often polymicrobial, but the most common microbial agent is *Staphylococcus aureus* that is included in the common skin flora in the healthy population. Unfortunately, MRSA (methicilin resistant *Staphylococcus aureus*) infections rate increases. The microbe is resistant to nearly all the other antibiotics, except of vankomycin (Kratochvíl et al. 2006).



Source: Rušavý et al. (1998)

Fig. 1. Pathogenesis of diabetic ulcerations

Examination methods

In addition to clinical condition assessment, many laboratory and imaging methods are used for precise diagnostics to determine the level and extent of the patient's disease with the diabetic foot syndrome.

Basic medical history data, we try to find out, is the diabetes type and its duration. Diabetes duration isn't decisive for the extremity amputation, as in 15–19%, diabetes mellitus is diagnosed only in a situation leading to an extremity loss (Piťhová 2008).

Furthermore, we determine the presence of the specific chronic complications (neuropathy, retinopathy), presence of cardial and vascular disease, possibly the undergone interventions. Further important medical history data are: smoking, lipid metabolism disorder, other serious general illnesses (liver, kidney illnesses, rheumatoid arthritis, psoriasis, even depressions). Social situation of the patient is of considerable importance, too – loneliness, low social level, homelessness, previous non-compliance.

Neuropathic problems are the subjectively serious ones (fornication, prickling, feet sweating disorders), resting pain or claudication pain, gait problems.

Clinical examinations: Via palpation, the physician determines the pulsation on the arteries, via auscultation, the presence of murmurs over big arteries. Then, the ankle-arm index is determined. Using the Doppler method, the blood pressure is measured on both arms in horizontal position, then on dorsal pedis artery and posterior tibial artery. Peripheral systolic blood pressure > 100 mm Hg indicates good blood perfusion of the extremities, values in the range of 50–100 mm Hg indicate a medium perfusion disorder. Chronic critical extremity ischemia is a disorder significant due to hematodynamics changes that developed gradually. It is defined by resting pain lasting for more than 2 weeks or ulceration or gangrene presence. Systolic ankle blood pressure is < than 50 mm Hg, systolic pressure on the thumb < than 30 mm Hg and the $TcpO_2$ < 10 mm Hg doesn't increase after oxygen inhalation.

If the absolute value of the ankle blood pressure is higher than 220 mm Hg or the ankle-arm index is > 1.25, medicalcinosis is present.

Laboratory examination: used in the diabetic patients with a diabetic foot can be divided into 3 groups:

1) Examinations monitoring the diabetes mellitus
   Glycemia is the basic monitored value, the target fasting glycemia is 4–6 mmol/l, postprandial glycemia 5–7.5 mmol/l.
   Glycated hemoglobin is a basic examination monitoring the long-term compensation of diabetes. The percent of the glycated hemoglobin reflects the glycemia for the last 2–3 months (target values are less than 4.5%).
   Further laboratory examinations are a detailed lipidogram, mineralogram, creatinine, urea, uric acid, hepatic tests (Haluzík 2009).

2) Examinations for inflammation monitoration
   The default objectification method is measuring of the body temperature, then blood count (leukocytosis, typical shift in the white cells differential), sedimentation – FW, C-reactive protein (a component of the non-specific humoral immunity) and procalcitonin (Kolář 2008).
   In diabetic foot syndrome, microbiology examination is very important. It is necessary to collect the material from the festering focuses for cultivation and sensitivity assessment repeatedly and carefully to avoid contamination.

3) Laboratory examinations performed in the pre-operative examination (Skalická 2007).

Imaging methods

An X-ray image of the foot in two projections to show osteoporosis, subchondral pseudocysts, spontaneous fractures or soft tissue edema. Complicating osteomyelitis leads to osteolyses and deformations in the bone structure and to subluxations (Lacman et al. 2005).

Ultrasonography examination allows both function (blood pressure measurement) and morphology examination of the arterial system. Using a two-dimensional ultrasonography imaging of the anatomy structures, it is possible to assess the arterial lumen and to find the stenoses and obstructions. Doppler techniques provide hemodynamic data about

the direction, speed and quality of the blood flow in the artery.

Arteriography of lower extremities is an invasive vascular examination indicated in clinical signs of the ischemic disease of lower extremities of IIb level (according to Fontaine) and more. The second indication for the invasive vascular examination is an ulceration without healing tendencies for 2–4 weeks of a complex therapy. Furthermore, every time before a planned amputation (Bartoš and Pelikánová 2000). Angiography is more and more replaced with the CT AG (CT angiography) and MRI (magnetic resonance imaging) angiography. After a diagnostic angiography, there is often a therapeutic procedure – percutaneous transluminal angioplasty (Chlup et al. 2005).

Scintigraphy using radionuclide-marked leukocytes is a suitable method. This method uses the fact that in the inflammation area of the organism, there is higher concentration of leukocytes. It is used to diagnose osteomyelitis in the patients with the diabetic foot syndrome. If a radionuclide is bound to the leukocytes, it is possible to determine the extent of the inflammation and extent of the tissue damage using a scintigraphy camera (differentiate the osteomyelitis from a soft tissue affection), to differentiate the Charcot's osteoarthropathy from an inflammation and to monitor the results of the treatment by repeating the examination (Kuníková et al. 2010).

Transcutaneous oxymetry is an effective non-invasive examination method using the polarography principle to determine the transcutaneous partial oxygen pressure ($TcpO_2$). The measured $TcpO_2$ value is a complex function of the skin blood circulation, metabolic activity, dissociation of the oxyhemoglobine and tissue oxygen perfusion (Gašpar et al. 2007).

In the patients with the diabetic foot syndrome, it is possible to objectify, using this method, the extremities ischemia level, as the other blood pressure measurement methods can indicate artificially high blood pressure values in the lower extremities in mediocalcinosis (Fife et al. 2009).

$TcpO_2$ value over 60 mm Hg is considered normal, the value under 30 mm Hg indicates a severe ischemia. It is not possible to assess only the absolute $TcpO_2$ value, you have to analyze the measured values ratio in a reference area and on the foot. According to the Transatlantic Inter-Society Consensus (TASC), the value 30 mm Hg stands for ischemia diagnosis and worse healing prognosis. However, the tolerance is 10 mm Hg, i.e. the healing is improbable in values under 20 mm Hg and almost sure in a value over 40 mm Hg.

Diabetic foot prevention

Many studies have shown that a complex feet-care can reduce the feet ulcerations amount by up to 50%.

The basics of diabetic foot prevention is regular checking of the feet and the shoes in every patient's visit at the treating physician and education of the patient every time.

A detailed screening examination according to the guidelines is to be performed at least 1× per year, in high risk patients more often.

During the regular feet inspection, it is necessary to focus on the skin defects – pressure sores, hyperkeratosis, blisters, ragades, mycoses, skin color and temperature changes, further on deformities and deformations. Shoes check should be a part of the examination!

Every inspection includes medical history data collection summing up, among others, a question about the previous education aimed at the feet care, question about walking barefoot, availability of the care, social situation, question aimed to detect neuropathy (prickling, sensitivity loss) and extremity ischemia (question about possible claudications).

Every year complete examination consists of arteries palpation on the lower extremities, including the dorsal pedis artery and anterior tibial artery, auscultation over the big arteries of the lower extremities.

Another examination using Semmes-Weinstein's monofilaments. It ise a 38 mm long nylon filament bending under the weight of 10 g. This very simple tool can help reveal a loss of the feet sensitivity. The filament is applied in 4 feet areas, insensitivity is proven, if the patient doesn't feel the touch in 6 points of the total 8 on both the feet. Further examination is using a tuning for or a biothesiometer that are able to reveal the loss of the vibration sensitivity. Dopplerometric examination of the pressure index – dorsal pedis artery/brachial artery is more and more

common. The norm is 1.0–1.4. The index lower than 0.9 indicates extremity ischemia and lower than 0.6 a critical ischemia.

The patients with a proven sensitivity loss, i.e. advanced neuropathy, are dispensed to a high risk group and can have the diabetic shoes prescribed. Patients with diagnosed extremities ischemia are indicated for angiography examination and the following intervention solution (committee of the Czech diabetologic organization 2012a).

Education

The education of the patient in prevention of the diabetic foot development is a never-ending process. Education that is not repeated loses its effectiveness. The education of the diabetic patients in prevention of the diabetic foot development consists of some basic points.

1) *Wear corrects shoes, never walk barefoot, not even at home.*
2) *Check your feet daily. If you are not able to see there, use a mirror or ask a family member for help.*
3) *Maintain correct hygiene standards – daily feet bath in lukewarm water.*
4) *Remove the rough skin with a pumice stone, use files when taking care of your feet, cut your nails straight after soaking in lukewarm water.*
5) *Do not forget that your feet don't feel warm, cold and pain well and protect them before possible injuries.*

The main target of the education is reaching a change in the patient's behavior. Education must be comprehensible, lively discussion is more suitable than a monotonous lecture. The best option is the combination of presented information with a written text allowing the patients to revise the obtained information at home. It is necessary to adapt the education for the target group, naturally in blind, poorly mobile diabetic patients, it is necessary to work with the family members. It is necessary to win the active cooperation of the patients so that they have their feet checked by the physician, because no checking of a diabetic patient can be considered as complete if the feet weren't checked (committee of the Czech diabetologic organization 2012b).

In the everyday contact with the patients who have lost their foot/leg, it is possible determine a mistake, easily to be seen a mile off, which, however, was the fatal mistake leading in its consequences to the extremity loss and that could be prevented in many cases if the care was correct.

Diabetic foot syndrome economy

The care of the patients with a diabetic foot syndrome is financially demanding for both the out-patient and the in-patient departments of the health care institutions. The treatment expenses can be generally divided into the direct, health care expenses (the work of the physician and using treatment products), direct non-healthcare expenses (activities of other kind than healthcare, connected with the treatment – e.g. the transport) and the indirect expenses, i.e. potential sources lost due to the disease (productivity loss due to inability, workload change, premature retirement, premature death). Not only antibiotics are financially demanding, but also the hospitalization and the diagnostic methods, or even seemingly low expenses as bandages of the defects by the nurses of the homecare services, transport with ambulance cars etc., if the problems last for months. The diabetology center in Plzeň tried to retrospectively quantify the half-year direct costs for health and social care (only the bandages by a homecare service are included) of a patient with the diabetic foot syndrome for the year 2000. It was on average 34,500 Czech crowns per patient per half a year.

In the diabetology center IKEM in the same year, the costs per a patient with a diabetic foot were about 2,800 Czech crowns per a day of hospitalization (without the angiography and vascular reconstruction procedures).

Hospital treatment of the defect cost 22,500 Czech crowns for a hospitalization of 26 days length on average. The total out-patient department care for one patient cost 7,250 Czech crowns (monitored for 8 months). The amputation cost 22,000 Czech crowns for 20 days of hospitalization on averages. Costs of compensation tools and social allowances were up to 400,000 Czech crowns in the first year after the amputation (Bruner and Anděl 2002).

Amputation

Periphery amputation

Toes amputation, even multiple, disturbs the stability of standing only minimally. In

the prosthetic care, shoe filling is sufficient. In toes amputation, at least a part of the proximal phalanx is preserved if possible, so that the other toes do not migrate to the emptied space. The hallux amputation doesn't significantly disrupt the foot stability as well. The load center is moved from the head of the 2nd metatarsus to the head of the 3rd toe metatarsus and the patient after the amputation tends to walk on the outer side of the foot.

High amputations

Crural amputations are performed at the border of the middle and the upper third of the shank. When correctly indicated and performed, total healing can be expected in 80% of the patients. The rehabilitation with a prosthesis is very good, up to 90% of the patients learn to walk.

Amputation over the knee joint is indicated in necroses passing the shank, in patients with polymorbidity leading to conclusion that they will not walk in future and in severe infections. It is possible to assume total healing in 90% of the patients after the amputation even in severe ischemia. Optimal level for the amputation, considering the seating of the prosthesis, is the border of the lower and the middle third of the femur. The longer the stump is, the higher the probability for a successful rehabilitation (Greppe and Kremer 1993).

Amputation stump adaptation is very important. An osteomyoplastic correction is performed. It is based on nerves preparation, extraction, preparation and resection as high over the osteotomy as possible so that they are out of the loaded part of the stump. This way, it is possible to prevent the "phantom pain". Technically correct adaptation of the resected bone is necessary too – the femur or the shank bones. The bone stump is then covered by a muscle-skin lobe that is turned from the back side in the thigh and shank area. After the surgery, the stump is formed in diabetic patients with a soft bandage. After complete healing, edema and pain decline, prosthetic treatment can be performed (Zeman et al. 1993).

Prosthetics

The prosthesis is a function and an esthetic replacement of the missing part of the extremity.

In the recent years, development of new technologies and materials used during production of artificial extremities replacements has significantly accelerated. It contributes to simpler, more reliable and comfortable usage of the prosthetic tools.

Social impact of the diabetic foot syndrome

Bio-psycho-social diabetes model extends the traditional biologic attitude to the illness and adds the personal and social aspects. A chronic diabetes complication – the diabetic foot syndrome – is a typical protracted illness, often requiring a long hospitalization or very often out-patient department visits. The diabetic foot treatment burdens not only the patients, but also the ones taking care of the patient. The quality of life of the patients (and not only of them) is mostly decreased by the wound care, poor mobility, often health care institutions visits and the fear of amputation (Nabuurs-Franssen et al. 2005). In a high amputation, working capability is not the only thing lost, often the patients are not self-sufficient anymore. Up to 20% of the patients worked and had a very active life at the moment of the diabetic foot syndrome development. Then, within a few weeks they became lost self-sufficiency and became dependent on social services.

With the illness onset:

- the working people lose their income;
- the expenses associated with the therapy increase;
- the travelling expenses (out-patient department bandages) increase;
- social expenses appear (due to inability to take care of himself/herself).

The most commonly applied form of social help are the allowances that can be divided into material and financial allowances and according to the length of the allowance provision – one-time or repeated (Kozlová 2005).

Luckily, the majority of the patients after the amputation have a family background (about 80 %) who can help the patient cope with the difficult situation (Krajcová 2005). Those patients who have no family background and are often people with a low social and economy level or seniors of high age use the homecare service and institutions of social care.

CONCLUSION

Diabetic foot syndrome is an illness affecting more and more patients. It is a cause for long suffering, long and expensive hospitalizations, furthermore a cause of invalidity, self-sufficiency loss and social care need.

It is a multidisciplinary problem that involves not only diabetologists-podiatres, but alos surgeons, angiologists, invasive radiologists, vascular surgeons and prosthetists and many other specialists, and last but not least all the diabetologists, education diabetologic nurses and general practitioners, since only education, prevention, active search for initial stages and their consistent therapy can avert the high amputation need.

The diabetic foot syndrome significantly influences the life quality of the patient in a negative way. Despite many preventive and therapeutic procedures, this complication increases morbidity, invalidity and mortality of the population.

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