

We are continuing to unlock the necessary insights so as to maximize “SANABUNA” (<http://www.crd-aida.ro/activitiespartnership/sanabuna-2011/>) opportunity initiatives, improving consumers/patients experience, including by making them aware of various risks, such as those revealed in the article below. We are pleased to allow researchers share their ideas and discoveries, ensuring our readers to get access to Health, Nutrition, Fitness and Wellbeing insights (<http://www.sanabuna.ro/the-second-international-congress-health-nutrition-fitness-and-wellbeing-for-central-southeast-europe-sanabuna-2012-took-place-on-the-19th-21st-october-at-the-art-museum/>), because we are all consumers/patients needing gaining better insights in order to take good decisions.

ASSESSING CLINICAL FINDINGS IN THE DIABETIC FOOT

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Abstract

Type 2 diabetes mellitus places an ever increasing cost on economies and patients' quality of life. One of this disease's complications is known as the diabetic foot. It refers to signs and symptoms that can be roughly classified in 3 groups: neuropathic, vascular and infectious. This review aims to list the most clinically-accessible signs and symptoms and to classify them according to their impact on quality of life in 2 groups: mild and severe.

Keywords: diabetic foot, clinical exam, complications

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INTRODUCTION

Diabetes mellitus (T2DM) is a frequently encountered disease in today's medical practice, and one of the fastest growing as well. This disease's impact has arisen almost simultaneously with the development of modern society; questions about modern lifestyle have started to be asked and be answered accordingly. It is estimated that a number of 592 million patients will be diagnosed with diabetes mellitus in 2035¹.

Factoring its costs paints a grim picture: as a permanent disease, patients often survive decades with gradually-worsening symptoms, complications and decreasing lifestyle quality. But, what is also important is the economic burden of diabetes: a 2012 study showed estimated costs of \$245 billion for treating T2DM patients in the US alone².

In this review, we are addressing the diabetic foot: a recently-described group of symptoms, spanning all diabetic complications that pertain to the inferior limb's most distal portion. We will focus on the clinical presentation of this syndrome and we will also be reviewing the relationship between these conditions. Finally, we will examine risk factors for the more serious diabetic foot complications. Pathophysiology of these lesions is beyond the scope of this article, being a complex field which warrants its own pieces of work instead.

REVIEW

T2DM is a disease with an unwavering course: sooner or later, complications hinder the life of every diabetic patient. Chiefly, diabetes induces multiorgan alterations that can be attributed primarily to excessive blood glucose, hyperglycemia. Out of these, the most frequent is neuropathy. After two decades of evolution, virtually all patients present with some degree of nerve affection. Other changes take place in the body's circulatory system: angiopathy of both the large and the small blood vessels, visible throughout the body, almost no organ spared.

How do these changes affect the inferior limb? As previously stated, T2DM complications can be roughly classified into either neurologic, vascular or infectious conditions, with the former two showing increased prevalence and earlier onset than the latter. This grouping is equally valid for the diabetic foot, which exhibits signs and symptoms of all categories. Most are non-life-threatening, thus warranting their inclusion in an appropriately-termed low-risk class; however, 4 of them carry a serious potential of decreasing quality of life or even being lethal: neuropathic arthropathy, ulcers, gangrene and amputation.

It has been shown that almost 85% of limb amputations are preceded by foot ulcers³. As usual, primary prevention is key - but, failing that, finding a practical way to predict ulcers would do much to elevate patient awareness and to sound an alarm. This high percentage validates an effort to attain means of secondary prevention of serious diabetic foot complications. Any such practical tool would have to be:

- Rapidly computable,

- Comprehensible for both physician and patient and
- Based on easily attainable analyses. This could include both laboratory parameters and clinical findings.

The rationale having been explained, we will begin describing the most frequent class of signs and symptoms, under the name of diabetic neuropathy. Some of the most common findings are the loss of tactile and vibratory sensitivity. At this stage, motor nerves are affected as well as proprioception. A turnkey point of further research would be to understand how many patients are aware of these changes, before being tested for them at the physician's request. Further in the evolution of T2DM, patients can also begin to lose thermal and pain sensitivity. The autonomous nervous system is affected next. Peripheral neuropathy in the absence of other complications has been shown to increase ulceration risk by 70%.

Among other clinically-evident complications of diabetic neuropathy there are cutaneous ones. Calluses, hyperkeratosis, and skin fissures appear frequently and share common causes. Chiefly, these multiple mechanisms can be attributed either to continuous microtrauma due to diminished tactile sensitivity, or foot deformation. Inappropriate footwear is a usually overlooked factor in this context. Half of all calluses are associated with an underlying foot ulceration, which can be discovered at a cursory glance by the presence of a hematoma. Hyperkeratosis can be usually found in the calcaneal area, along with fissures. Out of these 3 complications, hyperkeratosis was reported the most frequently, being observed in 27.1% of neuropathic T2DM patients. Calluses and fissures accounted for 3.7% and 3.5% respectively³.

Sympathetic nerve fibers are affected, which leads to sebaceous and sweat glands diminishing in size and atrophying. Clinical manifestations such as dehydrated skin and hair loss follow naturally. The same mechanism leads to another interesting and relatively rare finding (4%): neuropathic edema. This type of edema is defined as a diagnosis of exclusion, in the absence of cardiac, renal or venous failure. Its characteristics include normal local temperature, single- or two-sidedness, worsening with orthostasis. Increased

blood flow due to autonomic dysregulation contributes to the development of this edema, while also leading to venous insufficiency, as a result of varicose vein development.

Onychodystrophy or even nail atrophy may occur as a result of continuous trauma. Subungual hematoma can arise due to the same causes and is correlated with the degree of sensory loss.

The second group of diabetic foot complications spans two types of vascular affliction. Pathologically, atherosclerotic lesions (the first kind) have a greater extent and develop earlier in T2DM patients than in non-diabetic subjects. The other type of vascular damage has been described by Mönckeberg as calcification and sclerosis of the arterial tunica media. Vascular lesions arise both on large and small blood vessels.

Since these alterations take place at the tissue level, they cannot be minutely examined. Despite this, a reliable way to quantify arterial damage is the ankle-brachial pressure index. It has an elevated value, of more than 1.3, owing to vessel incompressibility. What can be found at a routine examination is diminished or absent popliteal pulse; the pedal pulse can suffer the same change.

Diminished or absent pulses can be ascribed to peripheral arterial disease. It may be present in any of the 4 L riche-Fontaine stages, with the expected signs and symptoms (discolored or cold skin, intermittent claudication, ischemic ulcers). Its prevalence increases from 15% at 10 to 45% at 20 years from T2DM diagnosis. It is important to differentiate ischemic from neuropathic ulceration: the former is painful, has a clear demarcation and is not surrounded by a callus. Its base is usually necrotic, and a necrotic crust can be found adhering to the surface. Sometimes, a neuropathic ulcer can develop in a patient with peripheral arterial disease, thus being termed ‘neuro-ischemic’.

Vascular complications also play a part in the aforementioned skin damage and hair loss, in addition to diabetic neuropathy. It has been shown that cutaneous blood flux is decreased in diabetic patients, as a result of arterio-venous shunt opening.

Wound healing capacity is gravely affected, both due to blood vessel deterioration and hyperglycemia affecting physiological functions of all the proteins involved in this process. Excess protein glycosylation leads to impaired function and increased healing time, readily apparent in the case of a diabetic foot ulcer. Additionally, 40% of patients have a recurrence within 1 year after healing, with up to 65% of ulcers reappearing in 5 years’ time⁴.

Abruptly-installed pain and edema may ensue in the presence of diabetic muscle infarction. This is a rare phenomenon, most frequently observed in the lower limb, in females, in T1DM and after 14 years of disease evolution. It has been surmised to occur due to diabetic arteriopathy.

Infections are the third major group of possible complications in diabetic foot patients. The most common is fungal disease, found in 38% of patients. Out of these, tinea pedis and onychomycosis, both caused by *Candida albicans*, are discovered most frequently. As for bacteria, *Staphylococcus aureus* is responsible for the majority of the bacterial infections, especially those associated chronic wounds. A recent study revealed significantly decreased bacterial diversity of the skin microbiome in diabetic patients, as opposed to non-diabetic controls⁵.

Any of the following forms of infection may be encountered:

- Skin or soft tissue infection (abscesses, necrotizing fasciitis)
- Cellulitis
- Acute osteomyelitis
- Chronic osteomyelitis

We will now continue with describing the second set of diabetic foot complications. As previously discussed, these are serious and should prompt the physician to warn the patient well in advance. In general, it is exceedingly hard to convince people about the nature of statistics in evidence-based medicine. It gets even harder when the subject is a future, potentially life-changing event, such as the amputation of a limb. Therefore, an instrument that would facilitate the patient’s understanding of this otherwise difficult-to-grasp concept would be immensely useful. A simple sheet of paper, color coded to represent various risk levels, has been put forth as a solution to fulfill this role. The inner

workings of such a system will remain the subject of an altogether different article.

To begin, foot ulcers are the most common serious T2DM complication. Typically, patients present with a profound skin ulceration, with the bottom of a pink color, surrounded by a callus, at the calcaneal level. It usually appears in typical high-pressure gait zone. No pain is associated with this lesion. Cellulitis or osteomyelitis can be discovered at the same time. The prevalence of foot ulcers in diabetic neuropathy patients has been reported as 3.5%. Out of all T2DM patients, it has been estimated that 15% experience foot ulcers at least once. It has been shown that primary prevention is 'very likely to provide cost-savings' for patients at moderate or high risk of diabetic foot ulcers⁶.

Foot ulcerations arising from sensory deprivation-related trauma have been termed 'neuropathic ulcers', as opposed to lesions that did not have prior nerve damage as a contributing risk factor. Diabetic foot ulcers can also have ischemia as pathogenic mechanism, or they can bear a mixed, neuro-ischemic origin.

Risk factors for the development of diabetic foot ulcers are:

- Infection
- old age
- diabetic neuropathy
- peripheral vascular disease
- smoking
- poor glycemic control
- previous foot ulcerations or amputations
- foot deformities
- renal failure
- impaired ability to look after personal care

Following foot ulcers, the so-called neuroarthropathy of the foot, or Charcot foot, is another grave development for T2DM patients. It is attributed to the loss of autonomic innervation, combined with an adequate degree of bone blood flow. This leads to osteopenia and decreased bone resistance, and is readily apparent through specific clinical findings.

Pes cavus, or high instep, along with claw toes lead to a deformed gait pattern and pressure redistribution. Thus, certain areas are exposed to

stress of a much higher degree. This is a decisive factor in trauma development, and indeed in the development of foot ulcers, in addition to infections. Any of the foot articulations may be affected.

Finally, gangrene is the endpoint of diabetic foot complications. It can develop de novo, following a traumatic event in several days (usually, at most 72 hours), or it can complicate a milder form of infection. It can be caused by aerobic bacteria (type A Streptococcus, Staphylococcus aureus) and anaerobic bacteria (Bacteroides, Enterobacter, Proteus). Ketoacidosis is a possible development.

Risk factors for gangrene include:

- Neuropathy
- Pathologic alterations of the large and small blood vessels
- The previously-described trauma-incurred skin lesions
- Diabetic retinopathy
- Loss of joint mobility
- Lack of patient education regarding diabetic foot lesions.

Taking all of these into account, the development of foot gangrene and subsequent amputation can only be regarded as failure of treatment.

CONCLUSION

Signs and symptoms of the diabetic foot may vary from patient to patient, but certain pathological processes are almost always present to some degree. It includes a range of signs and symptoms that we have tried to classify in mild or severe. The most common of the so-called benign findings is neuropathy. It is the starting point and a risk factor for most of the others. Most of the clinical signs are easy to discover and their pathogenesis is well-understood.

It is reassuring that the upsurge in diabetic patients has not been reported to be accompanied by a corresponding rise in the prevalence of complications. Patients still need to be made aware of the risks that high-severity symptoms entail, and ideally physicians should resolve this issue by introducing an easy to comprehend risk assessment method. Primary prevention has the potential to ease T2DM-derived economic burden

and increase patient quality of life by averting limb amputations.

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