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Review Article

DIABETIC FOOT ULCERS: IDENTIFICATION, DIAGNOSIS AND CURE

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ABSTRACT

Diabetic foot ulcers (DFUs) are a fairly common complication of diabetes. There are two forms: neuropathic ulcers and ischemic ulcers, although most DFUs are a mixture of both. Neuropathic Diabetic Foot Ulcers may come about because high blood sugar levels damage the nerves in your legs (called peripheral neuropathy). This means you are less likely to feel when you have injured your foot. The injury may be something as small and insignificant as a blister or a cut from walking with a stone in your shoe. If you can't feel the pain, then you do not know the injury is there and won't protect it and avoid walking on it. This makes it hard for the wound to heal. People with diabetes often suffer from poor blood circulation, especially to the legs (as part of a wider circulation problem called peripheral vascular disease). This means that it takes longer for your foot wounds to heal than for people with normal blood flow. This is Ischemic Diabetic Foot Ulcer. If a wound cannot heal, it is called an ulcer and it can become very serious. A diabetic foot ulcer presents a perfect way for germs and infection to enter your body. Infection can spread via the blood stream and enter into your bones. When this happens, the best, although drastic, action is to amputate the affected limb to stop gangrene spreading throughout your body. In the US and the UK, around half of all amputations are related to diabetes. Around half of people who have a leg amputated due to diabetes die within 5 years of the operation. This wouldn't need to happen if we had better foot care. Diabetic foot ulcer is one of the long standing complications of diabetic mellitus with the life time risk up to 25%. Many of the etiological factors contributing to the formation of diabetic foot ulceration may be identified using simple, inexpensive equipment in a clinical setting. Appropriate wound care for diabetic patients addresses these issues and provides optimal local ulcer therapy with debridement of necrotic tissue and provision of a moist wound-healing environment. The pathogenesis of foot ulceration is complex, clinical presentation variable, and management requires early expert assessment. Interventions should be directed at infection, peripheral ischemia and abnormal pressure loading caused by peripheral neuropathy and limited joint mobility.

KEYWORDS: Diabetes, Ulcer, Amputation, Assessment, Mortality.

INTRODUCTION

Diabetes, considered as a disease of developed countries, is one of the endocrine disorders that reached epidemic proportions worldwide[1]. The metabolic deregulation associated with diabetes mellitus (DM) cause's secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system [2]. Lots of complications are associated with DM. Those complications arise chiefly from the disruption of the vascular system which can result in inadequate circulation to the peripheral body. This places the foot at higher risk of ulceration and infection [3]. As the incidence of diabetes mellitus is increasing globally, increase in complications is also unquestionable. Overall all 15% of individuals with diabetes mellitus will have foot ulcer during their lifetime and the

annual incidence is 2-3% [4,5]. Diabetic foot ulcer is becoming major concern of diabetic patients and those who treat them from quality of life, social and economic stand point [6].

According to the 2005 international diabetic federation report 85%of diabetes-related lower extremity amputations are preceded by a foot ulcer. In developed countries one in every six people with diabetes will have an ulcer during their lifetime and even worst in developing. The annual incidence of diabetic foot ulcers is ~ 3%, and the reported incidence in U.S. and U.K. studies ranges as high as 10%.[7]

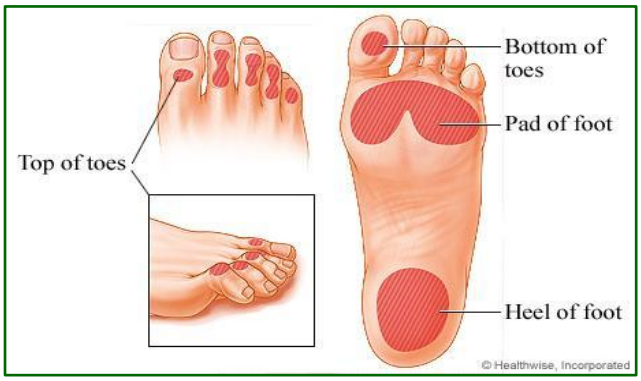

Figure 1: Areas affected by foot ulcer in a diabetic patient[3]

BACKGROUND

Diabetic foot ulcers, as shown in the image below, occur as a result of various factors, such as mechanical changes in conformation of the bony architecture of the foot, peripheral neuropathy, and atherosclerotic peripheral arterial disease, all of which occur with higher frequency and intensity in the diabetic population.

Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes. Diabetes is the leading cause of nontraumatic lower extremity amputations in the United States, with approximately 5% of diabetics developing foot ulcers each year and 1% requiring amputation.

Physical examination of the extremity having a diabetic ulcer can be divided into examination of the ulcer and the general condition of the extremity, assessment of the possibility of vascular insufficiency,[1] and assessment for the possibility of peripheral neuropathy.

The staging of diabetic foot wounds is based on the depth of soft tissue and osseous involvement.[2, 3, 4] A complete blood cell count should be done, along with assessment of serum glucose, glycohemoglobin, and creatinine levels.

A vascular surgeon and/or podiatric surgeon should evaluate all patients with diabetic foot ulcers so as to determine the need for debridement, revisional surgery on bony architecture, vascular reconstruction, or soft tissue coverage.

Cilostazol is contraindicated in patients with congestive heart failure. See Medication regarding the product's black box warning.

ETIOLOGY OF DIABETIC FOOT PROBLEMS

The main underlying risk factors for foot ulcers in diabetic patients are peripheral neuropathy and ischemia.

Neuropathy

Epidemiologic studies have found apoint prevalence of distal lower limb neuropathy ranging from 30% to 50% of the diabetic population studied.[11,12] Both type 1 and type 2 diabetic patients are similarly affected. With such frequent occurrence of neuropathy, it is no surprise that more than 60% of diabetic patients' foot ulcers are primarily due to underlying neuropathy.[13]

The distal neuropathy of diabetes affects all components of the nervous system: sensory, motor, and autonomic, each of which contributes to foot ulcer development. Loss of nerve function correlates with chronic hyperglycemia, as reflected in the mean level of glycosylated hemoglobin over time.[14] Ischemia of the endoneurial microvascular circulation induced by metabolic abnormalities from hyperglycemia is believed to be the underlying mechanism for nerve deterioration.[15,16]

Neuropathy in diabetic patients is manifested in the motor, autonomic, and sensory components of the nervous system. Damage to the innervations of the intrinsic foot muscles leads to an imbalance between flexion and extension of the affected foot. This produces anatomic foot deformities that create abnormal bony prominences and pressure points, which gradually cause skin breakdown and ulceration. Autonomic neuropathy leads to a diminution in sweat and oil gland functionality. As a result, the foot loses its natural ability to moisturize the overlying skin and becomes dry and increasingly susceptible to tears and the subsequent development of infection. The loss of sensation as a part of peripheral neuropathy exacerbates the development of ulcerations. As trauma occurs at the affected site, patients are often unable to detect the insult to their lower extremities. As a result, many wounds go unnoticed and progressively worsen as the affected area is continuously subjected to repetitive pressure and shear forces from ambulation and weight bearing.[17]

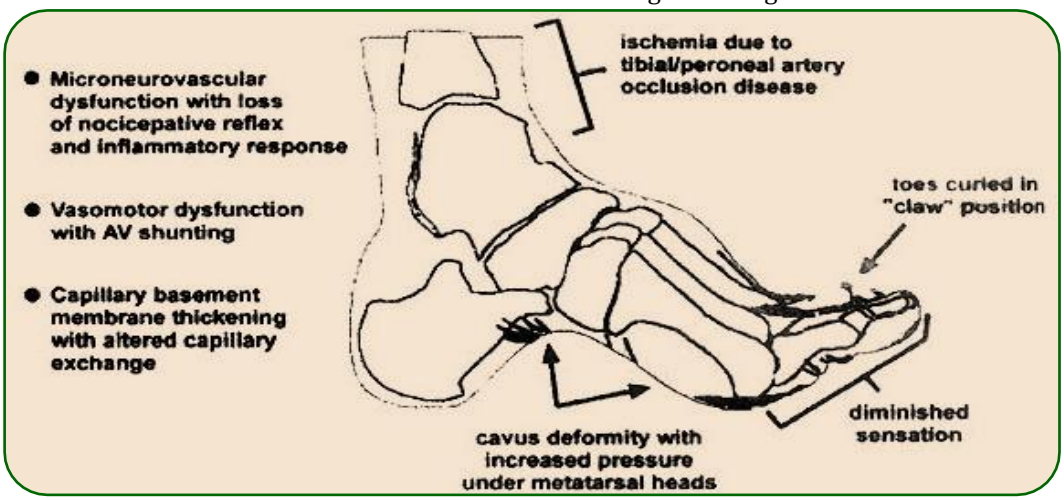

Figure 2: Common foot deformities resulting from diabetes complications: A) Claw toe deformity (increased pressure is placed on the dorsal and plantar aspects of the deformity as indicated by the arrow); and B) Cavus deformity (the rocker-bottom deformity leads to increased pressure on the plantar midfoot). [13]

Assessment of Diabetic Foot Ulcers

A task force of the Foot Care Interest Group of the American Diabetes Association (ADA) released a 2008 report that specifies recommended components of foot examinations for patients with diabetes.[12] Providers should take a history that takes

into consideration previous ulceration or amputation. The history should also include any neuropathic symptoms or symptoms that are suggestive of peripheral vascular disease. Further, providers should inquire about other complications of diabetes, including vision impairment suggestive of retinopathy and nephropathy, especially dialysis or renal transplantation. Finally, patients should be questioned regarding smoking because smoking is linked to the development of neuropathic and vascular disease. A complete history will aid in assessing the risk for foot ulceration.[13]

In examining the foot, visual inspection of the bare foot should be performed in a well-lit room. The examination should include an assessment of the shoes; inappropriate footwear can be a contributing factor to the development of foot ulceration. In the visual inspection of the foot, the evaluator should check between the toes for the presence of ulceration or signs of infection. The presence of callus or nail abnormalities should be noted. Additionally, a temperature difference between feet is suggestive of vascular disease.

The foot should also be examined for deformities. The imbalance in the innervations of the foot muscles from neuropathic damage can lead to the development of common deformities seen in affected patients. Hyperextension of the metatarsal-phalangeal joint with inter phalangeal or distal phalangeal joint flexion leads to hammer toe and claw toe deformities, respectively. The Charcot arthropathy is another commonly mentioned deformity found in some affected diabetic patients. It is the result of a combination of motor, autonomic, and sensory neuropathies in which there is muscle and joint laxity that lead to changes in the arches of the foot. Further, the autonomic denervation leads to bone demineralization via the impairment of vascular smooth muscle, which leads to an increase in blood flow to the bone with a consequential osteolysis. An illustration of some commonly described abnormalities is shown in Figure 2.

Pathophysiology

Atherosclerosis and peripheral neuropathy occur with increased frequency in persons with diabetes mellitus (DM).

Diabetes-related atherosclerosis

Overall, people with diabetes mellitus (DM) have a higher incidence of atherosclerosis, thickening of capillary basement membranes, arteriolar hyalinosis, and endothelial proliferation. Calcification and thickening of the arterial media (Mönckeberg sclerosis) are also noted with higher frequency in the diabetic population, although whether these factors have any impact on the circulatory status is unclear.

Diabetic persons, like people who are not diabetic, may develop atherosclerotic disease of large-sized and medium-sized arteries, such as aortoiliac and femoropopliteal atherosclerosis. However, significant atherosclerotic disease of the infrapopliteal segments is particularly common in the diabetic population. Underlying digital artery disease, when compounded by an infected ulcer in close proximity, may result in complete loss of digital collaterals and precipitate gangrene. The reason for the prevalence of this form of arterial disease in diabetic persons is thought to result from a number of metabolic abnormalities, including high low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) levels, inhibition of prostacyclin synthesis, elevated plasma fibrinogen levels, and increased platelet adhesiveness.

EPIDEMIOLOGY

According to the National Institute of Diabetes and Digestive and Kidney Diseases, an estimated 16 million Americans are known to have diabetes, and millions more are considered to be at risk for developing the disease. Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes. Among patients with diabetes, 15% develop a foot ulcer, and 12-24% of individuals with a foot ulcer require amputation. Indeed, diabetes is the leading cause of nontraumatic lower extremity amputations in the United States. In fact, every year approximately 5% of diabetics develop foot ulcers and 1% require amputation.

Age distribution for diabetic ulcers

Diabetes occurs in 3-6% of Americans. Of these, 10% have type 1 diabetes and are usually diagnosed when they are younger than 40 years. Among Medicare-aged adults, the prevalence of diabetes is about 10% (of these, 90% have type 2 diabetes). Diabetic neuropathy tends to occur about 10 years after the onset of diabetes, and, therefore, diabetic foot deformity and ulceration occur sometime thereafter.

Prevalence of diabetic ulcers by race

The issue of diabetic foot disease is of particular concern in the Latino communities of the Eastern United States, in African Americans,[10] and in Native Americans, who tend to have the highest prevalence of diabetes in the world.

PROGNOSIS

Mortality in people with diabetes and foot ulcers is often the result of associated large vessel arteriosclerotic disease involving the coronary or renal arteries.

Limb loss is a significant risk in patients with diabetic foot ulcers, particularly if treatment has been delayed.[11] Diabetes is the predominant etiology for nontraumatic lower extremity amputations in the United States. Half of all nontraumatic amputations are a result of diabetic foot complications, and the 5-year risk of needing a contra lateral amputation is 50%.[12]

In diabetic people with neuropathy[13] even if successful management results in healing of the foot ulcer, the recurrence rate is 66% and the amputation rate rises to 12%.

Patient Education

The risk of foot ulceration and limb amputation in people with diabetes is lessened by patient education stressing the importance of routine preventive podiatric care, appropriate shoes, avoidance of cigarette smoking, control of hyperlipidemia, and adequate glycemic control.

PHYSICAL EXAMINATION

Physical examination of the extremity having a diabetic ulcer can be divided into 3 broad categories:

- Examination of the ulcer and the general condition of the extremity.
- Assessment of the possibility of vascular insufficiency.
- Assessment for the possibility of peripheral neuropathy.

We should always remember that diabetes is a systemic disease. Hence, a comprehensive physical examination of the entire patient is also vital.

Examination of extremity

Diabetic ulcers tend to occur in the following areas:

- Areas most subjected to weight bearing, such as the heel, plantar metatarsal head areas, the tips of the most prominent toes (usually the first or second), and the tips of hammer toes (ulcers also occur over the malleoli because these areas commonly are subjected to trauma).
- Areas most subjected to stress, such as the dorsal portion of hammer toes Other physical findings include the following:
- Hypertrophic calluses
- Brittle nails
- Hammer toes
- Fissures

Assessment of possible peripheral arterial insufficiency

Physical examination discloses absent or diminished peripheral pulses below a certain level.

Although diminished common femoral artery pulsation is characteristic of aortoiliac disease, infrainguinal disease alone is characterized by normal femoral pulses at the level of the inguinal ligament and diminished or absent pulses distally. Specifically, loss of the femoral pulse just below the inguinal ligament occurs with a proximal superficial femoral artery occlusion. Loss of the popliteal artery pulse suggests superficial femoral artery occlusion, typically in the adductor canal.

Loss of pedal pulses is characteristic of disease of the distal popliteal artery or its trifurcation. However, be aware that absence of the dorsalis pedis pulse may be a normal anatomic variant that is noted in about 10% of the pediatric population. On the other hand, the posterior tibial pulse is present in 99.8% of persons aged 0-19 years. Hence, absence of both pedal pulses is a more specific indicator of peripheral arterial disease.

Other findings suggestive of atherosclerotic disease include a bruit heard overlying the iliac or femoral arteries, skin atrophy, loss of pedal hair growth, cyanosis of the toes, ulceration or ischemic necrosis, and pallor of the involved foot followed by dependent rubor after 1-2 minutes of elevation above heart level.

Assessment of possible peripheral neuropathy

Signs of peripheral neuropathy include loss of vibratory and position sense, loss of deep tendon reflexes (especially loss of the ankle jerk), trophic ulceration, foot drop, muscle atrophy, and excessive callous formation, especially overlying pressure points such as the heel.

The nylon monofilament test helps diagnose the presence of sensory neuropathy.[14] A 10-gauge monofilament nylon is pressed against each specific site of the foot just enough to bend the wire. If the patient does not feel the wire at 4 or more of these 10 sites, the test is positive for neuropathy. General use filaments can be obtained from the National Institute of Diabetes and Digestive and Kidney Diseases, or the clinician can use professional Semmes-Weinstein filaments.

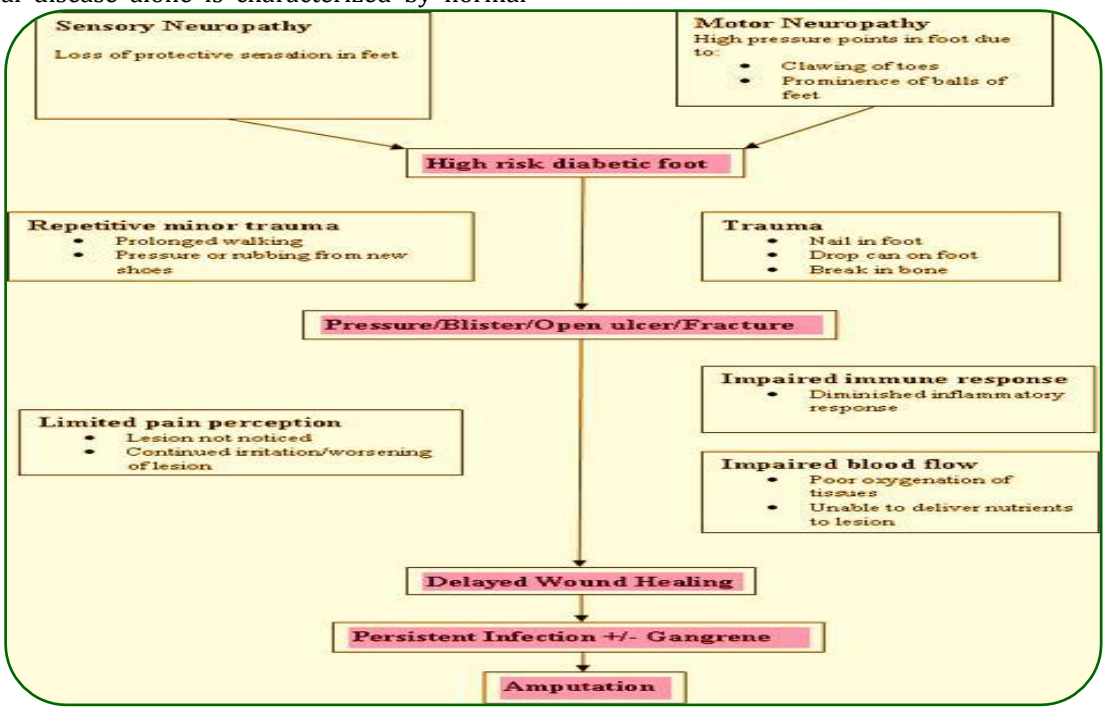

Figure 3: Features and symptoms of Diabetic Foot Ulcer [16]

PRINCIPLES OF MANAGEMENT

The first principle is to treat any infection; the second is to establish whether any associated ischaemia is amenable to revascularisation; the third is to keep forces applied to the ulcerated part to a minimum; and the fourth is to improve the condition of the wound or ulcer by wound-bed preparation, topical applications, and removal of callus. Once the wound has healed, attention can be turned to the prevention of ulcer recurrence.

Eradication of infection

The antibiotic regimen chosen should be based on the anticipated spectrum of infecting organisms. The combination of an aminopenicillin and a penicillinase inhibitor has the required activity, but other options include a quinolone plus either metronidazole or clindamycin.47,59 Intravenous options for soft-tissue infection include imipenem and gentamicin. Vancomycin, teicoplanin, rifampicin, or linezolid should be used for meticillin-resistant *S aureus*.[12,13]

The same broad-spectrum antibiotics are appropriate for osteomyelitis. Beta-lactams and quinolones are concentrated intracellularly at the site of infection, and clindamycin penetrates bones well. It has always been taught that infected bone should be removed, but a non-surgical approach might be effective.[15] The relative benefits of parenteral versus oral antibiotics are not known, but the parenteral route is preferred if the foot is severely ischaemic or in cases of systemic illness. Nor is the optimum duration of treatment known, though most clinicians opt for prolonged courses despite risks of inducing antibiotic resistance.[17]

Remediable macrovascular disease

Clinical evidence and positive non-invasive tests for macrovascular disease, such as an ankle/brachial pressure index below 0·8, toe systolic pressure of less than30 mm Hg, reduced transcutaneous oxygen tension, and abnormal duplex waveform on ultrasonography, indicate the need for assessment by a vascular surgical team. Options for revascularisation include angioplasty, thrombolysis, and bypass surgery. Distal bypass to the pedal vessels is increasingly common,[8,9] though with regional variations. Despite a huge increase in revascularisation procedures in the past 20 years, the effect on the rate of major amputation has been disappointing.[10] The potential benefit is clear, but the place of revascularisation has yet to be precisely defined.

PREVENTION

Primary prevention is the aim of diabetes management, but secondary prevention is the goal of good foot-ulcer care. The recurrence rate is high13 and ulcer healing should be followed by a well coordinated programme of secondary prevention. Sadly, this approach is beyond the capacity of health services in most countries. Surgery to correct deformities and abnormalities of posture, gait, andload-bearing74 (eg, lengthening the achilles tendon) has aplace in both primary and secondary prevention, but isprobably underused.

Primary prevention

Improved blood-glucose control will reduce microvascular complications, and reduction in cardiovascular risk factors will render the foot less susceptible to ischaemia from macrovascular disease. Routine surveillance will detect patients whose feet are at risk, and they should receive targeted care. Modelling indicates that this approach would be cost effective,[10] but primary prevention programmes have not always been beneficial.[13] The case for primary prevention might seem self-evident, but is not yet evidence based.

Secondary prevention

A previous lesion is strongly predictive for new ulceration.[7] Efforts should be made to reduce abnormal pressure loading, 74 which might involve cushioning in frail and immobile people and individually fitted footwear in those who are mobile, but such interventions need to be properly targeted.[11]Education should focus on foot care, regular podiatry, self-examination, and provision of emergency contacts. Education improves knowledge and illness-related behaviour,[12] and led in one trial to a three-fold reduction in re-ulceration and amputation within 13 months,[13] whereas McCabe and colleagues showed reduction in amputation but not in new ulceration. These findings require confirmation.[15] Educational effort might be more effective if aimed mainly at professionals.

CARE STRUCTURE

Successful management of diabetic foot ulcers requires close collaboration between many different groups in primary care and in the hospital service, and this collaboration might not be easy to establish while traditional barriers between health-care professionals remain in place. Supervision is also made difficult by the frequent coincidence of both social and medical problems, when the patient may be looked after by independent teams of professional carers. The needs and wishes of the patient (or his or her family) in influencing management choices are critical, and informed decisions by the patient should be an essential part of the process. Patients and carers should be counselled by trained health-care professionals at every stage, and should have ready access to a second opinion. The four-fold regional variation in incidence of major amputation reported both in the Netherlands and in the UK [14,15] suggests that patients are not always as informed and influential as they should be.

CONCLUSION

Foot ulceration is a common complication of diabetes that has potentially disastrous consequences for patients. Fortunately, better control of blood sugar levels, early recognition of complications of peripheral neuropathy and ischemia, and using a multidisciplinary approach to therapy when an ulcer develops can dramatically reduce this problem. Primary care physicians are key players in this approach when they identify diabetic patients at risk for ulceration and the ninitiate appropriate early management plans. Investment is urgently needed for basic research into the

pathophysiology of chronic wounds. Clinical management lacks a scientific basis and is determined by personal preference and the availability of local expertise and facilities. Therefore, clinicians should identify differences between centres, and undertake robust clinical trials of management, using appropriate end points. Speedy and effective care will be possible only with effective communication and collaboration between all relevant professionals. Many foot-care teams are described as multidisciplinary, but might still be restricted by traditional working practices.

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