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# Advances in treatment of diabetic foot ulcers*

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*References are only available in the online version of the article (www.avancesendiabetologia.org)*

## Abstract
Diabetic foot is a major health problem all over the world. Approximately 15% of the 200 million people with diabetes worldwide will develop a foot ulcer during their lifetime. Major amputation is a feared complication of diabetes. Many patients who undergo an amputation have a history of ulceration. More than 60% of non-traumatic amputations in the western world are carried out in diabetes patients. Major amputations increase morbidity and mortality and reduce the patient's quality of life. An important prelude to diabetic foot treatment is the differing diagnosis of neuropathic and neuroischemic foot. Treatment of a neuropathic plantar ulcer must correct pathological plantar distribution of pressures. Surgical treatment of deformities, with or without ulcerations, is an effective therapy. Charcot neuroarthropathy is a particular complication of neuropathy wich may lead to fragmentation or destruction of joints and bones. Additionally, in the diabetic population peripheral vascular disease (PVD) is the main risk factor for amputation. If PVD is not diagnosed, treatment of the ulcer cannot be successful. In diabetic patients PVD is distal, but often fully involves the femoral, popliteal and tibial vessels. It can be successfully treated with either open surgical or endovascular procedures. Finally, infection is a serious complication of diabetic foot. Phlegmon or necrotizing fascitis are not only limb-threatening problems, but also life-threatening ones. In this case emergency surgery is mandatory.

**Keywords:** diabetic foot, Charcot neuroarthropathy, foot ulcer, osteomyelitis, diabetic foot surgery.

## Introduction
Approximately 15% of diabetic patients experience a foot ulcer at some point in their lives.[1] More than 60% of non-traumatic amputations in the western world are performed in the diabetic population, with the incidence of major amputation varying from 0.5 to 5 per 1000 patients.[2,3] Morbidity and mortality rates are higher in patients with ulcerations. Mortality in the perioperative period is particularly high: reported to be 9% in a Dutch study[4] and 10-15% in the UK.[5] In a follow-up study of an amputated population, our group reported a 5-year survival rate of 50%.[6]

Diabetic foot must be considered a complex entity. Two types are recognized: neuropathic foot and neuroischemic foot.[7] The two entities have different pathophysiological mechanisms, diagnostic-therapeutic phases, and outcomes. There are different indications, different procedures and different organization of care in diabetic patients with neuropathic and neuroischaemic foot.

## The neuropathic foot
The association between peripheral neuropathy and foot ulcers is uniform in the literature.[8-12] Neuropathy is associated with an eight- to 18-fold increased risk of ulceration and a two- to 15-fold increased risk of amputation.[8,9]

The mechanisms through which neuropathy acts as a pathogenetic event for ulceration and, thus, amputation are complex and varied.[8-12] Above all, the reduction in protective sensitivity (including sensitivity to pain and heat) leads to a reduction in the perception of pain stimuli. Moreover, the motor component of neuropathy involves progressive weakening of the intrinsic muscle component, made up of interosseous and lumbrical muscles. This reveals itself as a deformation in toe flexion and the formation of overloaded plantar areas, identifiable under the metatarsal heads and the tips of the toes. Finally, the autonomous component of neuropathy causes anhydrosis and dry, flaky skin, as well as an increase in arteriovenous shunting, leading to altered skin and bone perfusion.

Proper debridement must follow the evaluation of an ulcer. This should completely remove the callus that surrounds the lesion and all non-healthy tissue, until healthy bleeding edges are revealed. Sharp debridement allows for thorough removal of all necrotic material and diminishes the bacterial load, thus promoting healing.[13-16] Although debridement of the ulcer is considered essential for the healing of diabetic foot ulcers, the grade of evidence is low.[17] However, this is likely to be related to the lack of studies rather than a lack of effect.

Subsequently, it is necessary to carry out an accurate "probe-to-bone" maneuver in order to establish any involvement of deeper structures such as tendons, joint capsules, and bones. In our opinion, in many cases the probe-to-bone maneuver with a sterile blunt instrument is adequate to diagnose osteomyelitis. Therefore, it is only necessary to use more complex methods (such as nuclear magnetic resonance and/or radio-labeled leuko-

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*List of acronyms quoted in the text:*
AT: Achilles tendon; BPG: by-pass grafting; CGRP: calcitonin gene-related peptide; CLI: critical limb ischemia; CN: Charcot neuroarthropathy; DPD: deoxypyridinoline; ICTP: carboxy-terminal telopeptide domain of type I collagen; IL-6: interleukin-6; MAC: medial arterial calcinosis; NOS: nitric oxyde synthase; NTX: N telopeptides of type I collagen; OPG: osteoprotegerin; PTA: percutaneous transluminal angioplasty; PVD: peripheral vascular disease; RANKL: NF-kB ligand; TASC: TransAtlantic Inter-Society Consensus; $TcPO_2$: transcutaneous oxygen tension; TNF-$\alpha$: tumor necrosis factor alpha.

**Figure 1.** Surgical treatment of a neuropathic plantar ulcer

**Figure 2.** Pan metatarsal head resection

**Figure 3.** Transmetatarsal amputation

cyte scanning) in a small percentage of cases.[18-24] A number of recent studies have questioned the reliability of the probe-to-bone test.[25,26] We entirely agree with the authors of these studies in the case that all patients are being considered and when the probe-to-bone test is being used as a screening tool. However, in "surgical patients" and in those with clinical signs of infection we still believe the maneuver is useful and reliable.

The literature clearly demonstrates that offloading is essential in cases of non-complicated plantar neuropathic lesions. Simple offloading techniques are multifaceted and include casts and boots, sandals, half-shoes, and felted foam dressings.[27-37]

Armstrong and Frykberg have provided a classification of diabetic foot surgery that correlates classes of treatment with a risk of amputation score.[38] The indications for surgical treatment of plantar neuropathic ulcers are essentially as follows:

- Coexistence of osteomyelitis.
- Plantar exostosis, which puts the healed wound at a high risk of recurrence.
- Chronically ulcerated wound resistant to conservative therapy.

In these situations, surgery allows two important results to be achieved: shorter wound healing time and surgical correction of the pathological overload by means of anatomical correction of the exostosis (figure 1).[39]

Piaggesi et al. have demonstrated that surgical treatment of a wound (ulcerectomy) accompanied by modification of the pathological overload (exostectomy) in a population of diabetic patients affected by plantar neuropathic ulcers allowed significantly shorter healing times and a lower rate of ulcerative repetition compared with conservative treatment.[14]

Microbiological assessment is performed to choose the appropriate antibiotic treatment before ulcerectomy. Appropriate specimens are obtained from the wound bed with a biopsy of the deep soft tissue. It is necessary to establish any involvement of bone (such as a metatarsal head) so as to plan the best type of surgery for the wound. Involvement of more than one metatarsal head or the presence of a vast plantar lesion may indicate the need for more complex surgical techniques, such as pan metatarsal head resection or minor amputation (figures 2 and 3).

Surgery should be not only curative but also effective in preventing new ulceration. Treatment of the overload by lengthening the Achilles tendon (AT) has been shown to be effective in reducing both the plantar pressures of the forefoot and the primary risk of ulceration and recurrent infection.[40]