CRITICAL LIMB ISCHEMIA

Updates in diagnosis
evidence and therapies
In the last ten years, all the most important medical companies have been investing a lot of efforts in order to project and develop dedicated devices for PAD endovascular treatment, with a particular attention to BTK and BTA lesions.

The new devices availability, together with the evolution of the endovascular techniques, allowed successful treatment of thousands of Italian patients with the clinical evidence of the efficacy of the multidisciplinary model, which is the main characteristic of the Italian tradition in the ischemic diabetic foot treatment.

This book is not only the result of a simple cooperation among different specialists but also a concrete example of the concept of multidisciplinary approach to this complex pathology.

At the same time, this book would like to highlight of our passion for this everyday job and our experience.

I would like to thank all the involved authors and teams and particularly Dr. Luis Mariano Palena, a great and tireless operator, for the priceless work done.

I hope that this book could help who wants to start the difficult path of this kind of treatment and above all, could give rise to a proper reflection for further studies: we still have a lot to learn!

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CRITICAL LIMB ISCHEMIA – Updates in diagnosis, evidence and therapies

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Diabetic people present a 12-25% risk of developing lifelong foot lesions.\(^1\),\(^2\)

The increasing diabetes incidence and prevalence, mainly in developing countries but also in Europe, makes foot lesions an actually relevant problem.

Foot ulcers can both cause the worsening of life quality and increase health costs. Furthermore, foot ulcers are the most important lower limb amputation risk factor,\(^3\),\(^5\) as more than 60% of non-traumatic amputations in the western world are performed in the diabetic population. The incidence of major amputations varies from 0.5 to 5 per 1000 patients.\(^6\),\(^7\)

Nearly 85% of all diabetes related lower limb amputations follow foot ulceration. In its “International consensus on the diabetic foot”, the International Working Group on Diabetic Foot defined diabetic foot as “a condition of infection, ulceration, and/or deep tissue damage” associated with neurological alterations and with several degrees of lower limb peripheral arteries disease.\(^8\)

Pivotal pathogenetic factors associated with diabetic foot are neuropathy and arteriopathy, besides reduced joints motility as an adjuvant factor and infection as a worsening factor. Furthermore, in most of the cases we can consider trauma as the inducing factor of lesions.

Based on the presence of different pathogenetic factors, we can divide ulcers into neuropathic, ischemic and neuroischemic;\(^9\),\(^10\) the International Consensus reported a percentage of 55% of neuropathic, 34% neuroischemic and 10% pure ischemic lesions.\(^8\)

**NEUROPATHIC ULCER**

Peripheral neuropathy plays a pivotal role on ulcer development and affects 80% of patients with foot lesions.\(^4\),\(^11\)

Diabetic neuropathy involves both sensitive and motorial and autonomic nerve fibres inducing different alterations implicated in the lesions’ genesis.

Sensitive neuropathy can reduce the ability to appreciate pressure or temperature variations, but it can mainly reduce the feeling of pain.

Pain is the first defence mechanism against foot damaging agents. The loss of protective sensibility, namely the loss of the ability to feel trauma which can induce skin lesions, plays an essential role in the development of most lesions.\(^12\)

Motor neuropathy causes atrophy and weakness of the intrinsic muscles of the foot; as a consequence, feet can present deformities which can lead to adipose lump dilocation and to the prominence of metatarsal heads. Under prominent metatarsal heads hyper-pressure areas can be found.\(^13\)

Autonomic neuropathy induces both a reduction of sweat secretions and artero-venous shunts to open. The loss of sweat causes the chapping and cracking of the skin, due to its dryness. The opening of shunts leads to foot warmth and, sometimes, swelling.

These situations can cause skin fragility and lesions as a consequence.\(^14\)

Besides neuropathy and vascular disease, in diabetic patients we can find a further factor which can play a role in the genesis of ulcers: joints’ mobility limitations, derived
from joint, soft tissues and skin protein glycation. Foot deformities, gait alterations, limited joint mobility are conditions which lead to foot biomechanical alterations with plantar pressures, all increase.

Due to the loss of pain sensibility, patients do not feel trauma generated by walk; in this way, under increased pressure areas skin reacts, producing corns.

Corns can act as a trauma, increasing 20-30 fold local pressures on skin; the corn induced mechanical stress produces subcutaneous bleeding and necrosis tissue and, ultimately, ulceration. These are the typical neuropathic ulcers, mainly localized in the plantar side.

In neuropathic pain-insensitive patients, lesions can occasionally arise apart from corn development, directly induced by mechanical, thermic or chemical stresses which ulcerate the skin.

It occurs, for instance, when a foreign body finds itself in the shoes or when patients wash themselves using hot water or manage their toe nails autonomously.

In these cases lesion location could be different from the plantar side, such as on the toe tip or on the back of the foot.

**ISCHEMIC ULCER**

Ischemia is the only clinical condition able to induce lower limb amputation per se, without the intervention of other risk factors.

In diabetic patients the risk of critical limb ischemia is fivefold higher with respect to non diabetic people.

Besides classical atherogenetic mechanisms, diabetes presents other factors that increase atherogenesis:

- the well-known lipid atherogenetic profile, with increased small-LDL and APO-B levels and hypertriglyceridemia;
- increased blood viscosity and coagulability due to higher fibrinogen and von Willebrand’s factor levels and reduced fibrinolysis;
- the main characteristics of peripheral vascular disease in diabetics are morphological and clinical findings. Obstructions are mainly located below the knee and occlusions prevail in comparison with stenosis; painful symptoms are frequently reduced or totally absent, due to sensitive neuropathy; medial arterial calcinosis is common.

The main problem of diabetic peripheral vascular disease is the suitability of diagnosis. The frequent absence of pain, both when walking and at rest, and the presence of arterial calcifications are confounding elements that often lead to an incorrect evaluation of some parameters, such as the ankle-brachial index and ankle pressure.

These typical diabetic characteristics are the main factors leading to an under-estimation of the presence of peripheral vascular disease, and this situation should play a pivotal role in delayed wound healing and the onset of gangrene.

An ischemic foot presents typical clinical features: atrophy of the whole foot (skin, muscles), reduction or absence of pedal and tibial pulses, thin and cold skin, paleness.

Peripheral vascular disease can cause serious lesions not necessarily derived by ulcerations, such as necrosis and wet gangrene. Typical ischemic diabetic foot expressions are gangrene of toes or forefoot, but the hind-foot is often involved too, with heel necrosis, mainly when patients are confined to bed.

Frequently, both neuropathy and peripheral vascular disease coexist in diabetic patients.

In these cases, clinical characteristics of the feet are a mixture of both conditions, with various degrees of deformity, lack of sensibility, cracked skin, absence of pulses. All these aspects can lead to ulcerations.
ACUTE INFECTIONS

Foot lesions may start as uncomplicated, but infection can develop and involve soft tissues and even bone, increasing the risk of amputation.\textsuperscript{25}

An infection’s local signs are inflammation, purulence, erythema, tenderness, warmth, lymphangitis; systemic symptoms such as fever, chills, acidosis, hyperglycemia, depicting a severe infection with systemic involvent, may be absent in up to 60% of cases,\textsuperscript{26} but they are key indicators of a limb-threatening and also life-threatening situation.

Since 1994 Caputo et al. \textsuperscript{27} described the clinical characteristics of diabetic foot infections, dividing them into three stages:

- \textit{non limb-threatening infections}: superficial lesions (no joint or bone involvement; no cellulitis or erythema ≤2 cm around lesion; absence of ischemia; mainly gram + agents;

- \textit{limb-threatening infections}: deep lesions (joint or bone involvement); superficial ischemic lesions; cellulitis or erythema >2 cm around lesion; lymphangitis; gram +/gram -/anaerobic agents;

- \textit{life-threatening infections}: deep lesions (joint or bone involvement); superficial ischemic lesions; cellulitis or erythema >2 cm around lesion; lymphangitis; gram +/gram -/anaerobic agents; systemic toxicity or metabolic instability (e.g., fever, chills, hypotension, leukocytosis, acidosis, hyperglycemia).

Foot anatomy is characterized by a compartmental model: three parallel cavities running along the foot, the median, medial and lateral, host tendons causing foot movements. Along these paths, infections can reach very rapidly both midfoot and hindfoot, but in the main they can go beyond the ankle and spread to the leg.

That’s why a deep foot infection which is not treated can easily lead to leg amputation.

ULCER CLASSIFICATION

Proper care of the diabetic foot ulceration requires a clear, descriptive classification system that may be used to direct appropriate therapy and possibly predict the outcome. Ideally, this system would be used by all participants in a multi-disciplinary limb salvage team.

A useful clinical classification system for diabetic foot wounds has to evaluate the wound depth, the presence of infection, and peripheral arterial occlusive disease in any category of wound assessment.

Up to 1996 the most considered classification was the Wagner classification.\textsuperscript{28} It was an anatomical classification identifying six lesion stages, based on the depth of the involved anatomical plane. It considered the presence of infections, too.

<table>
<thead>
<tr>
<th>Table 1-I</th>
<th>Texas University Wounds Classification.\textsuperscript{29}</th>
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<tbody>
<tr>
<td>Grade</td>
<td>Stage</td>
</tr>
<tr>
<td>A</td>
<td>Pre or post ulcerative lesion completely epithelialized</td>
</tr>
<tr>
<td>B</td>
<td>Infection</td>
</tr>
<tr>
<td>C</td>
<td>Ischemia</td>
</tr>
<tr>
<td>D</td>
<td>Infection and ischemia</td>
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Its hard limit is not considering peripheral vascular disease.

As limb ischemia is the prognostic factor mainly conditioning the evolution of lesions, it is important to be able to consider it when speaking of a lesion.

In 1996 Lavery and Armstrong published the “Texas University Wounds Classification”, considering both the anatomical and pathogenetic aspects of lesions.

Lesions are considered both for deepness and for the presence of infections and ischemia (Tab. 1-I).

The same authors demonstrated in 1998 a strict correlation between the lesion’s grade and stage and the risk of amputation.

REFERENCES


