Treatment Modalities Of Severe Diabetic Foot Infections
A Siegl, M Schintler, S Spendel, G Wittgruber, E Prandl, K Tiesenhausen, A Maier, E Scharnagl

Citation

Abstract
The most common cause of hospitalisation of diabetic patients is soft-tissue and bone infections involving the foot. Although many patients with severe infections are hospitalised and treated with intravenous antibiotics (IA), the role of early surgical management is often underrated and severe diabetic foot infections (SDFI) can become limb- or life-threatening events that may result in amputation of the lower extremity. Therefore we established our therapeutic strategies within the treatment of SDFI. 109 patients (1998-2000: 24 months) with SDFI (San Antonio: IID, IIIB, IIID) were retrospectively reviewed in the need for above-ankle amputation. Surgical debridement, treatment with IA, evaluation of the vascular status, hyperbaric oxygen therapy (HBO), vacuum-assisted-closure (V.A.C.®) and secondary reconstruction of the foot was performed.

In more than 80 % (94 patients) an amputation of the lower extremity could be avoided. In 15 patients (13.8%) an amputation of the lower extremity was performed. A combination of therapies including early surgical management, antimicrobial agents, the input of multiple specialists regarding the revascularisation of the foot and additional therapies like HBO and V.A.C.® are required, to avoid amputation of the lower extremity in SDFI in a large number of patients.

INTRODUCTION
The most common cause of hospitalisation of diabetic patients is soft-tissue and bone infections involving the foot [5,14]. Diabetic foot infections are frequently caused by a mixture of aerobic and anaerobic pathogens, with a majority of 60-70% due to gram positiv aerobics (s.aureus), 20-30% gram negativ aerobics (proteus spp., E. coli, Pseudomonas aeruginosa) and 4-15% anaerobic pathogens [8]. The main predisposing factors for the development of diabetic foot infections are macroangiopathy, microangiopathy, peripheral neuropathy and the altered immunological response of diabetic patients [14]. Many physicians who are not experienced with care for patients with diabetic foot infections tend to take the non-surgical approach. Although many patients with severe infections are hospitalised and treated with intravenous antibiotics, the role of early surgical management is often underrated. We think as other investigators [1,7,15], that this increases the patients risk for above-ankle amputation as well as not being cost-effective, because these patients are subjected to prolonged antimicrobial therapy without removal of the infected focus. Tragically the emergent nature of the problem frequently escapes the notice of diabetic patient and physician until it is too late to save the foot without partial amputation. Because systemic signs of infection are frequently absent or late, all infections must be treated aggressively. Early aggressive surgical intervention may prevent eventual limb loss, the need of above-ankle amputation, decrease total cost and may restore full ambulation earlier [14]. In other studies [14], any amputation- regardless of the level- was considered as treatment failure. Because limited amputation may restore the ability to function, we consider debridement and limited amputation as a part of the therapy. We use the endpoint of above-ankle amputation as treatment failure [14]. We reviewed our experiences with severe diabetic foot infections and analysed the influence of our therapeutic strategies on the need for above-ankle amputation.

MATERIAL AND METHODS
PATIENTS
Between 1998 and 2000 (24 months), a total of 109 diabetic patients (65 males and 44 females) with severe foot infections (San Antonio: IID, IIIB, IIID [1]) requiring hospitalisation were retrospectively reviewed (Tab. 1). Mean age was 55 years (33-86 years). The mean duration of diabetes was 22 years (8-35 years), the mean time of former
therapy of foot lesions until the arise of SDFI was 2,5 years (6 months- 4 years). In the majority of the cases (72%) foot ulceration was present, whereas in 30% a neglected minor trauma was the source of the infection. 73 Patients (67%) presented with sensory polyneuropathy (PNP) whereas in 36 patients (33%) a combination of peripheral arterial occlusive disease (PAOD) and sensory polyneuropathy was found.

**Figure 1**
Table 1: Symptoms in 109 patients with SDFI (before hospitalisation)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>4</td>
</tr>
<tr>
<td>Oedema</td>
<td>15</td>
</tr>
<tr>
<td>&quot;Probe to bone&quot;</td>
<td>7</td>
</tr>
<tr>
<td>Deep without osteomyelitis</td>
<td>3</td>
</tr>
<tr>
<td>Gangrene</td>
<td>3</td>
</tr>
<tr>
<td>Ulceration</td>
<td>8</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>6</td>
</tr>
<tr>
<td>Hyperleukocytosis</td>
<td>6</td>
</tr>
<tr>
<td>Deep abscesses</td>
<td>7</td>
</tr>
<tr>
<td>Lymphangiectasis</td>
<td>5</td>
</tr>
</tbody>
</table>

**LABORATORY TESTS**
Routine haematological and biochemical tests, x-rays, aerobic and anaerobic cultures of the deep wound were performed in all patients.

**SURGICAL DEBRIDEMENT**
Complete drainage, unroofing all abscessed cavities and repetitive debridement of necrotic tissue as soon as possible (within 24 hours after hospitalisation) was carried out and repeated within a two day period if necessary (Tab. 2). After debridement patients were kept on bed rest to allow further dependent drainage and reduction of oedema [4,7].

**Table 2: Surgical Interventions, n=109**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of performed procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Debridement of necrotic tissue</td>
<td>327</td>
</tr>
<tr>
<td>Amputation of digit</td>
<td>167</td>
</tr>
<tr>
<td>Excision of ulcers</td>
<td>270</td>
</tr>
<tr>
<td>Draining of abscessed cavities</td>
<td>364</td>
</tr>
<tr>
<td>Partial amputation of the foot (transmetatarsal, Chopart)</td>
<td>37</td>
</tr>
<tr>
<td>Above-knee amputation</td>
<td>15</td>
</tr>
<tr>
<td>Total No. of surgical interventions in all 109 patients</td>
<td>1109</td>
</tr>
</tbody>
</table>

**MICROBIOLOGY ASSESSMENT / ANTIBIOTIC THERAPY**
Aerobic and anaerobic cultures of the deep wound or debrided tissue (bone) were performed prior to the initiation of the parenteral antibiotic treatment and were repeated every week. All patients received Fosfomycin (200mg/kg KG /24h) in combination with Clindamycin ( Dalacin® 3x600mg) or Ciprofloxacin (Ciproxin® 3x200mg) or Amoxicilin/Clavulan-acid (Augmentin® 3x2,2g) for at least 14 days.

**VASCULAR ASSESSMENT OF THE LOWER EXTREMITY**
The evaluation of the vascular status of the lower extremity was performed in all patients by a vascular surgeon. Arteriography was performed in all patients with critical limb ischaemia and those who underwent amputation (Tab . 3).

**Figure 3**
Table 3: Vascular assessment and vascular surgery in 36 patients (32% of 109 patients) with PAOD and PNP

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of patients with PAOD and PNP</th>
<th>% of patients with PAOD and PNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography</td>
<td>14</td>
<td>100%</td>
</tr>
<tr>
<td>Amputation</td>
<td>10</td>
<td>100%</td>
</tr>
<tr>
<td>Amputation of the foot (transmetatarsal, Chopart)</td>
<td>7</td>
<td>1.74</td>
</tr>
<tr>
<td>No successful neurovascularisation</td>
<td>15</td>
<td>22%</td>
</tr>
</tbody>
</table>

**HYPERBARIC OXYGEN THERAPY (HBO)**
HBO- therapy was performed in a multiple- person chamber through selection of transcutaneous PO₂ (TcPO₂) measurement within the first session. If it was >35 mm Hg, HBO- therapy was continued until complete healing of the
wound with 2.5 ATA / 60 min every day [4]. The mean sessions of HBO were 14 (9-18).

VACUUM- ASSISTED- CLOSURE (V.A.C.®)

V.A.C.® – treatment was applied on every patient after debridement and totally absence of necrotic tissue with continuous suction of 125 mm Hg. The V.A.C.® system was changed every 2-3 days [1]. The mean time of V.A.C.® application was 10 days (8-12 days).

SECONDARY RECONSTRUCTION

With skin grafts or flaps depending on the local situation (Tab. 4).

RESULTS

INFECTION TYPES

Similar to other investigators, we found that the forefoot was the most common site of infection in diabetic patients. Neuropathy, not vascular insufficiency, is the major predisposing factor of foot infections [14]. Additionally, the high prevalence of osteomyelitis (Tab.1) that was found among the patients, especially in the forefoot, is similar to that reported in recent trials [16,14]. The polymicrobial character of diabetic foot infections in our patients definitely confirm the findings of other studies [7,13,16].

RESULTS OF THERAPY

In more than 80 % (94 patients) of the 109 patients an amputation of the lower extremity (above-ankle) could be avoided. In 15 patients with PAOD (13,8%) an amputation of the lower extremity was necessary after revascularisation could not be performed successfully. In 21 patients with PAOD (78% of 36 patients), revascularisation was performed after the initial debridement (Tab. 3).

The mean sessions of HBO were 14 (9-18). The mean time of V.A.C.® application was 10 days (8-12 days). In our patients the mean number of debridements were 2 (1-4). The average length of hospital stay were 15 (10-19 days). In 77 patients the first reconstructive procedure after debridement was successful. In 17 patients further surgical interventions (debridement and skin graft) were necessary to restore the foot (Tab. 4).

DISCUSSION

This retrospective review in our patients, involving a follow up time of nearly 2 years in a significant number of diabetic patients with severe infections of the lower extremity (San Antonio: II D, III B, III D), could provide some guidelines in the management of such infections [4].

Severe diabetic foot infections require immediate hospitalisation and a combination of surgical management with non-surgical therapies regardless of haematologic parameters or hyperglycaemia [15,12]. Surgical management of limb- threatening infections is vital and begins with complete drainage and debridement of necrotic tissue according to the IRAS –principles (treating the infection, revascularisation, (minor) - amputation, orthopaedic shoes) reported by Vollmar et al.1986 [16]. When possible, care should be taken to preserve as much of the foot structure as feasible to allow functional weight-bearing [11] once the infection has resolved. Multiple debridements may be necessary to provide adequate drainage and control of infection. In our patients the mean number of debridements were 2 (1-4) which is in accordance with the data reported by other investigators [16].

Similar to the results reported in other studies [16], limb salvage in many cases is dependent upon restoring perfusion to an ischemic foot, but sepsis must be controlled prior to any attempts of revascularisation. When infection is too severe that the foot is nonviable or when life- threatening sepsis is present, open amputation of a ray, foot or leg may be the initial procedure of choice. After thorough drainage and debridement, the patient must be kept on bed rest to allow further dependent drainage and reduction of oedema [7,13].

Additionally, intensified non-surgical therapies should be carried out. As in other studies [16], polymicrobial character of most diabetic foot infections is almost invariable when these infections become deep-seated. Many pathogens identified in diabetic foot infections are resistant to commonly prescribed antimicrobial agents [4]. This fact points out the need of aerobic and anaerobic coverage. Because of the vascular impairment in these patients, antibiotic delivery to sites of infection may be reduced. Thus
enhancing the necessity for drugs with extensive tissue penetration even to the bone. Maier et al. showed the high tissue penetration of Fosfomycin® in combination with other antibiotics. According to our results combining Fosfomycin® with Ciprofloxacin, Clindamycin or Amoxicillin/Clavulan-acid for at least 14 days, showed excellent results in the treatment of severe diabetic foot infections.

Vascular insufficiency is one of the predisposing factors of foot infections. The evaluation of the vascular status of the lower extremity should be performed in all patients after the initial debridement by a vascular surgeon (Tab.3). In our patients revascularisation was performed in 21 patients (78%) with PAOD after initial debridement. In 15 patients (22%) revascularisation failed which made an amputation (above-ankle) necessary.

Although hyperbaric oxygen therapy (HBO) is discussed controversy within the literature and controlled studies are lacking in this regard, however, we suggest as reported by Kindwall et al. and other investigators, that HBO might be of great benefit for SDFI in stimulating angiogenesis, increase the capillary ingrowth, enhance the bactericidal effects of leukocytes (respiratory burst), decrease rigidity of the red cells, and reduce the number of average debridegments. Systemic hyperbaric oxygen greatly increases tissue oxygen levels and these values remain elevated for several hours after exposure. In our setting, HBO-therapy was performed in a multiple- person chamber through selection of the TcPo measurement during the first set. If it was >35 mm Hg, HBO-therapy was continued until complete healing of the wound with 2,5 ATA / 60 min every day. The mean sessions of HBO were 14 (9-18).

For preservation of the wound a V.A.C.® – system was applied on every patient after debridement and total absence of necrotic tissue with continuous suction of 125 mm Hg. The V.A.C.® system was changed every 2-3 days (1,13). As shown by Argenta et al. and other investigators, this allows a continuous elimination of the superficial secretion, an additional reduction of oedema and pathogen microbials and stimulation of wound healing. In our patients the mean time of V.A.C.® application was 10 days (8-12 days).

Secondary reconstruction was performed depending on the local situation of the foot with either skin grafts, local flaps or free flaps. In 77 patients the first reconstructive procedure after debridement was successful. In 17 patients further surgical interventions (debridement and skin graft) were necessary to restore the foot (Tab. 4).

In our study the average number of surgical interventions (2 times) and the average length of hospital stay (15 days) confirms data reported by other investigators in the treatment of SDFI. As mentioned, the purpose in the management of severe diabetic foot infections is to preserve and restore foot function. Our concept was not analysed with regard to reduce hospitalisation and the cost. This may be the case as well because patients will be able to ambulate earlier and return to work, but to decrease the above-ankle amputation rate (between 92% and 100%) in patients with SDFI. If revascularisation is not successful in patients with PAOD, an amputation of the lower extremity cannot be avoided after all (Tab.3).

CONCLUSION

The increasing population of diabetic patients resulted in a greater number of diabetic foot infections. Management of these infections especially in severe cases require a thorough knowledge of the involved factors and current diagnostic and treatment regimens. As shown in our retrospective study, a combination of therapies including early surgical management, antimicrobial agents, the input of multiple specialists regarding the revascularisation of the foot and additional therapies like HBO and V.A.C.® are required to avoid amputation of the lower extremity in severe diabetic foot infections in a large number of patients. But without the initial early debridement any non-surgical approach alone is going to fail.

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References
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