



# Two-Step Sequential Approach for Concomitant Skin and Soft Tissue Infection and Osteomyelitis Complicating the Diabetic Foot

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Current guidelines (1,2) do not provide data on the treatment of patients presenting with concomitant soft tissue infection and osteomyelitis of the diabetic foot (DF-STI/DFO). We have developed a two-step sequential approach (TSA) consisting chronologically of 1) an empirical antibiotic therapy for diabetic foot soft tissue infection (DF-STI) secondarily adapted to the culture results of a tissue sample taken by curettage from the periphery of the ulcer (step 1), 2) an antibiotic-free period of at least 2 weeks, and 3) a bone biopsy obtained percutaneously or intraoperatively in case of, respectively, medical or surgical approach of diabetic foot osteomyelitis (DFO) (step 2) chosen according to Lipsky's recommendations (3). In the present monocentric retrospective 2006–2015 study, 38 adult patients out of a total of 297 patients followed for DFO (12.8%) had concomitant DF-STI and DFO not requiring urgent surgery and were treated with TSA. DFO was determined by clinical elements (bone exposed through the ulcer, positive probe to bone test) and imaging data on plain X-rays, bone scans, or MRI. Antibiotics administered for DFO were chosen among those with a high bone-to-blood ratio associated with

sustained activity against biofilm bacteria and good oral availability, such as rifampin and fluoroquinolone combinations for, respectively, gram-positive cocci and gram-negative bacilli osteomyelitis (4,5). Remission of DFO was defined as the absence of recurrence of both DF-STI and DFO at the initial infected site or contiguous to it, complete healing of the foot ulcer, and no need for additional surgery during the post-end of treatment follow-up. Approval by the local ethics committee was obtained (no. 2017/1). The patients' main characteristics are reported in Table 1. All patients had peripheral neuropathy, and six of them (15.8%) who were found at admission to have associated ischemia of the foot on the basis of clinical findings confirmed by angiography underwent with success either endoarterial stent placement or arterial revascularization.

The average duration of the empirical antibiotic treatment of DF-STI was  $23.1 \pm 7.8$  days and mostly comprised  $\beta$ -lactam agents. DFO management consisted of conservative surgery in nine (23.7%) patients and minor amputations in seven (18.7%). DFO was confirmed via bone culture results for all patients, including a bone sample obtained percutaneously

for the 22 patients treated medically. During the interval between the initial admission and the management of DFO, worsening of bone abnormalities on plain X-ray imaging was seen in eight patients (enhanced bone erosion was present in all cases). No changes in the therapeutic approach of DFO (i.e., medical vs. surgical) decided at the initial admission were made at step 2, including in those patients with worsening bone abnormalities between step 1 and 2. After a mean follow-up of  $3.9 \pm 2.1$  years, 26 (68.4%) patients were in remission. Remission was associated with the use of rifampin and fluoroquinolone combinations (Table 1).

Besides the retrospective design of the current study and the small population size, our results suggest that TSA allows for respect of the basic rules for the antibiotic treatment of both soft tissue infection and osteomyelitis of the foot in patients presenting with concomitant DF-STI and DFO without impairing the outcome of DFO.

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**Table 1—Comparison between remission and failure patients treated for concomitant DF-STI and DFO with the TSA: univariate analysis**

Variables	Total population (n = 38)	Favorable outcome (n = 26)	Unfavorable outcome (n = 12)	P
Age, years	65.4 ± 11.3	63.8 ± 12.2	68.9 ± 8.2	0.19
Male/female	24/12	18/8	6/6	0.25
BMI, kg/m <sup>2</sup>	31.1 ± 5.76	30.9 ± 6.8	31.5 ± 5.6	0.83
Duration of diabetes, years	16.1 ± 5.2	14.7 ± 7.1	18.7 ± 11.6	0.28
HbA <sub>1c</sub> at admission, % (mmol/mol)	7.6 ± 1.1 (171 ± 24.8)	7.5 ± 1.2 (169 ± 27.1)	7.7 ± 0.6 (174 ± 13.6)	0.71
Previous amputation of the foot	17 (44.7)	12 (46.2)	5 (41.7)	0.79
Fever at initial admission	4 (10.5)	3 (11.5)	1 (8.3)	0.76
DFO located at the forefoot	21 (55.2)	12 (46.2)	9 (75)	0.10
Duration of DF-STI Abx, days	22.8 ± 15.4	23.4 ± 17.7	21.4 ± 16.1	0.86
Antibiotic-free period before step 2, days	31.1 ± 16.9	30.4 ± 9.2	31.7 ± 9.7	0.34
Duration of DFO Abx, days	64.8 ± 32.6	67.6 ± 35.6	56.3 ± 23.5	0.71
Surgical treatment of DFO	16 (42.1)	9 (34.6)	7 (58.3)	0.17
<i>Staphylococcus aureus</i> DFO	21 (55.2)	14 (53.8)	7 (58.3)	0.80
GNB DFO	16 (42.1)	9 (34.6)	7 (58.3)	0.17
Rif or FQ combination for DFO Abx	22 (57.9)	18 (69.2)	4 (33.3)	0.04

Data are mean ± SD or n (%) unless otherwise indicated. Abx, antibiotic treatment; FQ, fluoroquinolone; GNB, gram-negative bacilli; HbA<sub>1c</sub>, glycated hemoglobin; Rif, rifampin.

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