Six-Week Versus Twelve-Week Antibiotic Therapy for Nonsurgically Treated Diabetic Foot Osteomyelitis: A Multicenter Open-Label Controlled Randomized Study

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OBJECTIVE

Little is known about the optimal duration of antibiotic therapy for diabetic foot osteomyelitis (DFO). This study sought to compare the effectiveness of 6 versus 12 weeks of antibiotic therapy in patients with DFO treated nonsurgically (i.e., antibiotics alone).

RESEARCH DESIGN AND METHODS

This was a prospective randomized trial comparing 6- versus 12-week duration of antibiotic treatment. Remission of osteomyelitis during the monitoring period was defined as complete and persistent (>4 weeks) healing of the wound (if present initially), absence of recurrent infection at the initial site or that of adjacent rays, and no need for surgical bone resection or amputation at the end of a follow-up period of at least 12 months after completion of antibiotic treatment.

RESULTS

Forty patients followed at five French general hospitals were randomized between January 2007 and January 2009, with 20 treated for 6 weeks and 20 treated for 12 weeks with antibiotics. The two groups were comparable for all variables recorded at inclusion in the study. Remission was obtained in 26 (65%) patients, with no significant differences between patients treated for 6 versus 12 weeks (12/20 vs. 14/20, respectively; *P* = 0.50). We did not identify any significant parameters associated with patient outcome. Fewer patients treated for 6 weeks experienced gastrointestinal adverse events related to antimicrobial therapy compared with patients treated for 12 weeks (respectively, 15 vs. 45%; *P* = 0.04).

CONCLUSIONS

The present multicenter prospective randomized study provides data suggesting that 6-week duration of antibiotic therapy may be sufficient in patients with DFO for whom nonsurgical treatment is considered.

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The question of whether diabetic foot osteomyelitis (DFO) can be successfully treated without removing the infected bone remains subject to debate. It had long been thought that removal of the infected bone was necessary for arresting chronic bone infection since success rates reported in older reports using antimicrobial therapy alone had been disappointing (1). Interestingly, more recent clinical studies have shown that DFO can be arrested in selected patients using antibiotic therapy without bone resection (2–7). However, the optimal duration of antibiotic treatment of osteomyelitis complicating foot wounds in non–surgically treated diabetic patients is currently unknown (1). International guidelines recommend ≥3 months of antibiotic therapy in the absence of surgery or in case of residual dead bone after surgery (8). Antibiotic use encourages antimicrobial resistance, incurs financial cost, and may cause drug-related adverse effects. Rifampin and fluoroquinolones achieve high bone concentrations and have an antibacterial activity that is maintained against stationary phase bacteria, as seen in chronic osteomyelitis. The use of rifampin and fluoroquinolones in this setting may therefore help decrease the treatment duration. A recent study found that antibiotic therapy, mainly rifampin combinations, directed by bone culture results (compared with empiric antibiotic therapy) was associated with a significantly higher rate of remission of bone infection after a mean of 12 months of follow-up (9). A reduction in treatment duration might help to alleviate drawbacks of the medical approach in these patients. We therefore conducted a randomized multicenter clinical study, the goal of which was to compare the effectiveness and tolerance of 6- versus 12-week antibiotic therapy in patients with DFO treated nonsurgically using rifampin or fluoroquinolone combinations as first-line therapy.

RESEARCH DESIGN AND METHODS

Population

We conducted a prospective randomized multicenter study comparing 6- versus 12-week durations of antibiotic treatment in diabetic patients treated nonsurgically (i.e., without amputation or resection of the infected bone) for osteomyelitis of the foot complicating a neuropathic foot without peripheral arterial disease that was assessed by clinical examination and complementary investigations. Patients were excluded in case of absence of both anterior and posterior pedal pulses with Doppler arterial examination showing significant stenosis or occlusions. In case of persisting doubt, transcutaneous oxygen pressure examination was used to assess the existence of a critical ischemia (<30 mmHg). Patients 18 years old or over were included if they had type 2 diabetes and osteomyelitis of the foot (i.e., below the ankle).

Osteomyelitis was suspected when at least two of the following clinical criteria were present: a wound lasting ≥2 weeks over an underlying bony prominence, with an ulcer surface ≥2 cm^2 or depth ≥3 mm, associated with probing to bone and/or abnormalities consistent with a diagnosis of osteomyelitis on plain radiographs, bone scans (coupled gallium [^{67}Ga-citrate]-technetium [^{99m}Tc-diphosphonate] radionuclide or LeukoScan [sulesomab scintigraphy using an anti-granulocyte antibody Fab fragment labeled with ^{99m}Tc]), or MRI. In addition, it had to be confirmed by a positive culture of a transcutaneous bone biopsy performed after an antibiotic-free period of at least 2 weeks as described earlier by our group (10). Patients who had gangrene and who required bone resection because of bone and/or joint destruction or amputation due to severe peri-osteoarticular damage were not included.

Treatment

Empirical antibiotic treatment was prescribed while waiting for culture results if physicians considered it necessary. Antibiotics adapted to bone culture results were started as soon as definitive results were available. Antibiotics were selected based on patient comorbidities and were prescribed at doses adapted from those proposed by Spellberg and Lipsky (11). For gram-positive cocci infections, rifampin was used in combination with (by decreasing order of preference) levofloxacin, trimethoprim-sulfamethoxazole, doxycycline, linezolid, or any other antimicrobial agent active against bone pathogens for the entire duration of treatment. For gram-negative bacilli infections, levofloxacin or ciprofloxacin was used in combination with cefotaxime, ceftriaxone, or cefepime for the first 2 weeks of treatment and then continued for the rest of the treatment as monotherapy. The companion for rifampin and levofloxacin or ciprofloxacin was chosen according to the susceptibility profile of the bone pathogens and patient characteristics. Antibiotics were administered either orally for the entire treatment period or intravenously for a short period (5 to 7 days) followed by a long course of oral antimicrobial therapy. A computerized random number generator centralized at Dron Hospital of Tourcoing was used to generate the random allocation sequence (i.e., 6- vs. 12-week duration of antibiotic therapy). Renal, hepatic, and hematologic parameters were assessed during treatment. The imputability of adverse events related to the antibiotic treatment was assessed according to the chronology of the onset of events, the need for reducing the daily dosage of the incriminated antibiotic, the data from any attempt to reintroduce the incriminated treatment, and the type of recorded toxicity (e.g., tendonitis and myalgia for levofloxacin and drug-drug interaction for rifampin). To be attributable to a given antibiotic, a reduction in the daily dosage and/or a discontinuation due to intolerance had to be recorded in the patient's medical chart.

All physicians adopted a standardized approach to debridement and wound care, which included use of alginates, hydrocolloids, or hydrogels. Patients were not treated with topical antimicrobials or other adjunctive therapy. Removing pressure from the infected wound using a suitable device was also recommended.

Outcome Assessment

The primary outcome measure was the proportion of patients of each group with remission of DFO defined as *1*) the absence of any local and systemic sign of infection, *2*) stabilized or improved radiographic abnormalities on plain X-rays assessed at the end of treatment and 1 year later, and *3*) complete sustained healing of the wound responsible for the underlying osteomyelitis. In addition, remission had to have no relapsing infection or need for surgery at the initial site or the contiguous rays during a posttreatment follow-up period of at least 12 months. Failure was defined as any other

outcome. The secondary outcome measure was the number of episodes of adverse events attributable to the antibiotic treatment recorded in each group of patients.

Statistical Analysis

In the initial analysis of data, all variables were stratified according to patient outcome (i.e., remission or failure). We performed a comparison of continuous variables, e.g., patient age at enrollment, with a two-sample *t* test and categorical variables such as sex using a two-tailed Fisher exact test. The significance level was set at $P < 0.05$. Statistical analyses were conducted using Stata software version 7.0. Written consent was obtained for each included patient.

The investigations were carried out in accordance with the principles of the Declaration of Helsinki. The present prospective randomized study (ClinicalTrials.gov, NCT02123628) was approved by the Committee for Protection of Persons Involved in Biomedical Research of Lille University Hospital (1 February 2007) and the French Agency for Safety of Health Products (15 March 2007).

RESULTS

Five investigational centers located in Northern France participated in the current study (Arras, Bethune, Douai, Lens, and Tourcoing). The study completion date was September 2012. During the inclusion period lasting from June 2007 to June 2010, 211 patients were seen for a suspicion of DFO, among whom 53 met the inclusion criteria. Thirteen patients were not included in the study since transcutaneous bone biopsy was sterile in 11 of them, and two additional patients refused to give written consent. Ultimately, 40 patients met study criteria and were included in the current study. The main characteristics of the included patients are summarized in Table 1. The duration of diabetes was 10 years or more in 28 patients (73%). Nine patients (22.5%) had previously undergone minor or major amputation of the foot for infectious reasons before enrollment. The foot wound was located on a metatarsal head in 28 patients (70%) and on a phalanx in 12 patients (30%). According to University of Texas wound classification, 24 patients (60%) were graded 3; according to the perfusion, extent/size, depth/tissue loss, infection, and sensation classification, infection was graded 3 in 36 (90%) patients and 4 in the 4 remaining patients. The mean duration of the foot wound before inclusion was 19.7 ± 17.5 weeks.

Plain radiographs of the foot were performed in each patient and showed abnormalities consistent with diagnosis of osteomyelitis in all but two of them. In an imaging assessment, the most frequent abnormalities seen on plain radiographs of the foot were subchondral lucency (n = 23; 57.5%), cortical erosion (n = 13; 32.5%), and periostal reaction (n = 2; 5%). Four patients (10%) underwent computerized tomography and another patient MRI, all of whom showed signs of osteomyelitis. No significant difference was found between patients treated for 6 versus 12 weeks regarding all studied parameters, including those that were not compared in Tables 1 and 2.

Staphylococcus aureus was the predominant organism cultured from bone samples, followed by coagulase-negative staphylococci and gram-negative bacilli, which accounted for 22.5% of pathogens (Table 2). Polymicrobial infections were seen in 18 (45%) cultures. Methicillin-resistant *S. aureus* strains were identified in seven patients (17.5%), all susceptible to rifampin.

Transcutaneous bone biopsy was performed by an orthopedic surgeon at the operating theater for 26 patients (65%) and by a radiologist in the interventional radiology room for the other patients, depending on the center where patients were recruited. No adverse events related to bone biopsy obtained using a radiological or surgical method were reported.

In total, 30 patients (75%), 14 (70%) from the 6-week group and 16 (80%) from the 12-week group, were hospitalized for a mean duration of 9.2 days (range 1 to 30), with no significant differences between the two groups of patients (10.3, range 1 to 30, vs. 8.7 days, range 1 to 20; P = 0.98). Empirical antibiotic treatment using mostly oral coamoxiclav was prescribed while waiting for culture results in 18 (45%) patients. Pathogens isolated from bone biopsy were resistant to the empirical antibiotic therapy in 4 of these 18 patients (22%), 1 in the 6-week group and 3 in the 12-week group. The documented antibiotic therapy was begun with a median delay of 14 days (range 5 to 19) after bone biopsy, by the parenteral route in 18 patients (45%) for a median duration of 8 days (range 6 to 9). Rifampin was the antibiotic agent most frequently used (27 patients; 67.5%), followed by fluoroquinolone (especially levofloxacin) in 28 patients (70%). The combination of rifampin and a fluoroquinolone was administered in 19 patients (47.5%) (Table 1). Antibiotic-related adverse events were recorded in 16 patients (40%), 6 (30%) from the 6-week group and 10 (50%) from the 12-week group; the most common adverse events were of gastrointestinal origin, all attributable to rifampin, including three episodes in patients from the 6-week group versus nine episodes in patients from the 12-week group (P = 0.04) (Table 3). Other adverse events included skin allergy (n = 2), drug-drug interactions (n = 1), dizziness (n = 1), acute renal insufficiency (n = 2), and thrush (n = 1), without any significant differences between the two groups of patients (data not shown).

At the end of a mean posttreatment follow-up duration of 12 months, 26 patients (66%) were considered to be in remission, 12 (60%) from the 6-week group and 14 (70%) patients from the 12-week group (P = 0.50) (Table 4). At final examination, plain radiograph was unchanged in 29 patients (72.5%), including 25 remission patients, and was considered as normal in 1 remission patient. Worsening radiological abnormalities were seen in 10 failure patients, including cortical erosion (n = 3), periosteal reaction (n = 3), subchondral lucency and sclerosis (n = 2), and bone fragmentation (n = 2). Reasons for failure are presented for each group of patients in Table 4. Nonhealing of the wound at the end of follow-up was recorded in 6 of the 14 failure patients, 2 (10%) and 4 (20%) patients treated for 6 and 12 weeks, respectively (P = 0.38). Among the eight failure patients who had completely healed, five (two treated for 6 weeks and three for 12 weeks) had a relapsing osteomyelitis due to the occurrence of a new ulcer at the initial infected site, and three other patients had a worsening radiological outcome that led us to consider these three others as failure patients, in accordance with our definition criteria for remission.

We did not identify any parameter associated with the patient outcome including methicillin-resistant *S. aureus*

Table 1—Characteristics of patients from each group

	All patients *n* = 40 (%)	6 weeks *n* = 20 (%)	12 weeks *n* = 20 (%)	*P*
Sex ratio, female/male	11/29	5/15	6/14	0.72
Age, years, mean ± SD	64. 2 ± 10.5	64.6 ± 11.2	63.8 ± 10.9	0.81
Diabetes-related complications				
Retinopathy	22 (55)	9 (45)	13 (65)	0.20
Nephropathy	20 (50)	10 (50)	10 (50)	1
Neuropathy	38 (95)	20 (100)	18 (90)	0.15
Coronary artery disease	10 (25)	5 (25)	5 (25)	1
Malnutrition[a]	8 (20)	3 (15)	5 (25)	0.43
Fever (>38°C) at admission	4 (10)	2 (10)	2 (10)	1
Wound surface, mm^2, mean ± SD	9.8 ± 6.0	11.4 ± 6.9	8.5 ± 5.7	0.33
Positive probe-to-bone test	19 (47.5)	7 (35)	12 (60)	0.11
Location				
Metatarsal head of the first ray	8 (40)	3 (15)	5 (25)	
Metatarsal head of the fifth ray	10 (25)	7 (35)	3 (15)	
Other metatarsal locations	14 (35)	6 (30)	8 (40)	
Hallux	8 (20)	4 (20)	4 (20)	0.37
C-reactive protein, mg/L ± SD	16.5 ± 18.1	12.2 ± 15.6	20.9 ± 24.2	0.19
Leukocytes, G/L ± SD	7,677.4 ± 2,657.3	7,542.7 ± 2,948	7,827.1 ± 2,367	0.74
Polymorphonuclear leukocytes, G/L, mean ± SD	5,099.5 ± 2,004.1	5,037.3 ± 2,034.1	5,165.3 ± 2,028.4	0.84
HbA_{1c}, % (mmol/mol), mean	8.12 (65)	7.90 (63)	8.35 (68)	0.43
Creatinine blood level, mg/L, mean ± SD	10.6 ± 3.97	10.75 ± 4.36	10.42 ± 3.64	0.80
Methicillin-resistant *S. aureus*	7 (17.5)	3 (12)	4 (20)	0.67
Rifampin	27 (67.5)	15 (75)	12 (60)	0.31
Fluoroquinolone (levofloxacin or ciprofloxacin)	28 (70)	14 (70)	14 (70)	1
Rifampin + fluoroquinolone	19 (47.5)	11 (55)	8 (40)	0.34

All data are at enrollment and are number of adverse events (%) unless otherwise indicated. [a]Defined as one or more among the following: weight loss ≥10%, BMI ≤17 kg/m^2 (age <70 years) or ≤20 kg/m^2 (age >70 years), albuminemia <30 g/L or prealbuminemia <110 mg/L.

infection, which was associated with remission in five out of seven patients (71.4%). Patients with or without postbiopsy empirical antibiotic therapy had similar failure rates (6/18 [33.3%] vs. 8/22 [36.7%], respectively; *P* = 0.84).

Table 2—Microbiology of bone sample cultures in 40 diabetic patients with osteomyelitis of the foot

Pathogens	Overall (%) total number of strains = 58	6 weeks (%) total number of strains = 30	12 weeks (%) total number of strains = 28	*P*
Gram-positive cocci	48 (82.7)	24 (80)	24 (85.7)	0.73
S. aureus, total	20 (34.5)	8 (26.7)	12 (42.8)	0.27
S. aureus resistant to methicillin	7 (12.1)	3 (10)	4 (14.3)	0.70
Coagulase-negative staphylococci	17 (29.3)	9 (30)	8 (28.6)	1
Streptococcus spp.	2 (3.4)	1 (3.3)	1 (3.6)	1
Enterococcus spp.	6 (6.9)	4 (13.3)	2 (7.2)	0.67
Corynebacterium spp.	3 (7.5)	2 (6.7)	1 (3.6)	1
Gram-negative bacilli	9 (15.5)	5 (16.7)	4 (14.3)	1
Pseudomonas aeruginosa	2 (3.4)	1 (3.3)	1 (3.6)	1
Proteus spp.	4 (6.9)	2 (6.7)	2 (7.2)	1
Escherichia coli	2 (3.4)	2 (6.7)	0	0.49
Morganella morganii	1 (1.7)	0	1 (3.6)	0.48
Obligate anaerobes	1 (2.5)	1 (3.3)	0	0.48
Polymicrobial infections	18/40 (45)	10/20 (50)	8/20 (40)	0.75

Data are number of patients (%).

CONCLUSIONS

The results of this study suggest that 6-week duration antibiotic therapy for DFO treated nonsurgically is associated with an outcome similar to that of 12-week duration. This is the first prospective randomized study to date that has addressed this question. The duration of antibiotic therapy for DFO treated without resection of the infected bone tissue remains traditionally based on prolonged administration of ≥12 weeks (11). However, there is no evidence that antibiotic therapy for >6 weeks improves cure rates, as no randomized trials compared different durations of antibiotic treatment for DFO or for any other sort of chronic osteomyelitis (12). According to the recent Infectious Diseases Society of America guidelines, antibiotic therapy should be continued for 6 to 12 weeks if infected bone or soft tissues remain despite surgery (8). According to the same guidelines, antibiotics should be maintained for 12 weeks or more in patients for whom the resection of infected and

Table 3—Antibiotic-related gastrointestinal adverse events reported in 40 diabetic patients with DFO treated nonsurgically according to the duration of antibiotic therapy

Antibiotic-related adverse events	6 weeks *n* = 20	12 weeks *n* = 20
Nausea	1 (5)	2 (10)
Vomiting	1 (5)	2 (10)
Diarrhea	0	2 (10)
Hepatic cytolysis/cholestasis	1 (5)	3 (15)
Total	3 (15)	9 (45)[a]

Data are number of patients (%). [a]*P* = 0.04.

necrotic bone could not be done for any reason (8).

This prospective randomized study confirms the possibility of treating selected diabetic patients with osteomyelitis of the foot without surgery. A recent prospective randomized study conducted by Lázaro-Martínez et al. (7) showed that antibiotics and surgical treatment have similar outcomes in patients with neuropathic forefoot ulcers complicated by osteomyelitis without ischemia or necrotizing soft tissue infections. According to the Infectious Diseases Society of America guidelines, surgical treatment of osteomyelitis is not necessary when *1*) surgery would cause unacceptable loss of function, *2*) there is an untreatable limb ischemia, *3*) the infection is confined to the forefoot with minimal soft tissue loss, or *4*) surgery is considered inappropriate or undesirable by the patient and health care professional (8). The medical approach to DFO is often criticized for collateral damage due to antibiotic use, especially the emergence of bacterial resistance, but also adverse events, in particular, *Clostridium difficile*–associated diarrhea (CDAD), along with significant cost (1). In this study, gastrointestinal adverse events were reported in significantly more patients receiving 12 weeks of antibiotic treatment than in those receiving only 6 weeks, but the use of rifampin combinations in the majority of our patients (27/40; 67.5%) may have influenced these results. The absence of any reported case of CDAD in our patients is consistent with the low incidence of CDAD episodes described in patients treated with rifampin, especially in a setting of tuberculosis (13). Reduction in the length of antibiotic courses appears to be the best strategy for effectively limiting antibiotic resistance by reducing the selective pressure on bacterial flora, but the design of this study did not allow for addressing this question (14,15).

The overall remission rate of 65% in our patients assessed at least 1 year after the end of treatment is comparable to the results established in previous studies (2–7,9). It is, however, difficult to compare the remission rates reported in the literature since, to date, there exists no consensus concerning remission criteria for DFO. We used hard remission criteria, which included the assessment of both the healing of the foot ulcer and the evolution of bone involvement. Indeed, the best way to assess the outcome of DFO has not yet been clearly defined (16). It is crucial that complete and sustained healing of the ulcer occurs, as it prevents against any new foot infection and represents a strong argument against the existence of an active underlying DFO (17). On the other hand, it also seems important to assess the radiological outcome of the initial bone abnormalities and to report the occurrence of relapsing episodes of DFO during a posttreatment follow-up period of at least 1 year, as recommended for any other type of chronic osteomyelitis. In our study, the proportion of patients with relapsing DFO at the end of 1 year of posttreatment follow-up was 15%, which is similar to that reported by Tice et al. (18). The percentage of our patients who required major amputation during follow-up (10%) was comparable to the results reported by Embil et al. (14%) (6), Korda et al. (5%) (19), and Margolis et al. (6.7%) (20). The overall proportion of patients in whom complete healing was obtained was 85%, with a mean healing time of 15 weeks, slightly shorter than the 26 weeks reported in the study by Kessler et al. (21). Univariate analysis did not identify any parameter associated with the patient outcome, especially methicillin-resistant *S. aureus*–related infections, which is consistent with a previous study from Aragón-Sánchez et al. (22).

The median delay of 14 days between bone biopsy and the beginning of the documented antibiotic therapy in our patients is due to the fact that we waited for the definite results of bone culture (i.e., 14 days) before starting the documented antibiotic treatment. Indeed, rifampin combinations are the first antibiotic choice in our center for the treatment of staphylococcal osteomyelitis of the foot and are debuted only when the definite results of bone culture are available (i.e., between 10

Table 4—Clinical outcome of 40 diabetic patients with osteomyelitis of the foot treated nonsurgically according to the duration of antibiotic therapy

Patient outcome	6 weeks *n* = 20	12 weeks *n* = 20	*P*
Overall remission	12 (60)	14 (70)	0.50
Complete healing[a]	18 (90)	16 (80)	0.38
Time to complete healing (weeks ± SD)	13.1 ± 12.2	16.8 ± 17.4	0.44
Overall failure	8 (40)	6 (30)	0.50
Noncomplete healing	2 (10)	4 (20)	0.37
Relapsing osteomyelitis	2 (15)	3 (15)	1
Worsening radiological bone abnormalities	6 (30)	4 (20)	0.46
Bone resection	2 (10)	2 (10)	1
Spread of osteomyelitis to contiguous sites	4 (20)	2 (10)	0.37
Major amputation	2 (10)	2 (10)	1

Data are number of patients in whom the event was recorded (%). The total number of each column may exceed the total (overall failure), since more than one event may be recorded in a given patient. [a]Complete healing of wound sustained for at least 4 consecutive weeks.

and 14 days). Indeed, empirical administration of rifampin combinations was discouraged in the investigating centers in order to limit the risk of treating the patient with a monotherapy of rifampin (in case the pathogens are resistant to the rifampin companion) and therefore to promote the emergence of rifampin-resistant strains (23,24). This delay may appear surprising, but we think that DFO is not an indication for urgent antibiotic therapy, especially in patients with no signs of inflammation of the foot, which was the case in 22 (55%) of our patients (17). Moreover, patients in this study treated with or without empiric antibiotics after bone biopsy while waiting for the microbiological results had a similar outcome ($P = 0.84$).

The strength of the current study is that all of the included patients had initial radiographic bone abnormalities consistent with the diagnosis of osteomyelitis that were confirmed by bone culture results. We only used transcutaneous bone biopsy performed with proper precautions in order to limit the risk of false-positive results, although this doubt is difficult to eliminate (16). Bone biopsy was done after an antibiotic-free period of at least 2 weeks in order to reduce the risk of false-negative results. We did not perform histological testing on bone samples due to its difficult interpretation and failure to provide better diagnostic information than microbiological study according to recent studies (25,26). In addition, patient outcome was assessed at least 1 year after the end of treatment as generally done in other types of chronic osteomyelitis (27).

Several methodological weaknesses may have affected the validity of our results. First, comparisons were made on small numbers, and therefore the risk of error leading to the absence of differences in the compared populations is high. Second, identification of failure cases may not have been optimal because of the follow-up duration, which did not exceed 1 year. The results of the current study therefore warrant a further larger-scale study in order to assess other beneficial effects of a reduction in duration of antimicrobial therapy for DFO, especially with respect to the emergence of bacterial resistance and antibiotic-related adverse effects.

In conclusion, the present multicenter prospective randomized study provides data suggesting that a 6-week duration of antibiotic therapy may be sufficient in patients with DFO treated without removal of the infected bone and is associated with better gastrointestinal tolerance in a setting of predominant use of rifampin combinations.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.
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