



Treating Diabetic Foot Osteomyelitis Primarily With Surgery or Antibiotics: Have We Answered the Question?

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Foot infections are among the most frequent diabetes-related causes for hospitalization and the usual immediate predecessor to lower-extremity amputation in these patients (1).

Infection usually starts in ulcerated soft tissues, but can spread contiguously to underlying bone (2). Overall, about 20% of patients with a diabetic foot infection (and over 60% of those with severe infections [3]) have underlying osteomyelitis, which dramatically increases the risk of lower-extremity amputation (4). Indeed, optimally managing diabetic foot osteomyelitis is widely considered the most difficult and controversial aspect of dealing with diabetic foot infections (5–7).

In the preantibiotic era, the only option for treating osteomyelitis was surgical resection of all necrotic and infected bone. Because surgeons feared further spread of infection up the limb in what was then called “diabetic gangrene,” most procedures were major (often above the knee) amputations (8). The advent of antibiotic therapy led to a marked reduction in both mortality (9–11) and need for major amputations (10,11) in patients with diabetic foot infections. Antibiotic therapy was largely considered adjunctive to surgery, but in the past two decades reports appeared of patients with diabetic foot osteomyelitis apparently

cured by antibiotic therapy with little or no surgical resection (12), leading some to reexamine the belief that surgery was almost always needed for this form of chronic osteomyelitis (13).

There are potential advantages, as well as disadvantages, to both medical and surgical treatment of diabetic foot osteomyelitis (Table 1). In some clinical situations, it is clear that one or the other approach is most appropriate (Table 2), but in most cases the question of which approach should be selected for any individual patient has been difficult to answer based on robust evidence. Available studies, all of which

are case series with key design flaws, have demonstrated reasonably good outcomes with either initial conservative surgery (14–16) or initial medical therapy (17–19); the choice was often based on the specialty training and preferences of the treating clinician. Recently published guidelines on managing diabetic foot infections illustrate the current state of uncertainty. Those produced by the International Working Group on the Diabetic Foot suggest “available studies do not provide information to inform which cases [of diabetic foot osteomyelitis] may require surgery”

Table 1—Potential advantages and disadvantages of initial primarily surgical or primarily medical treatment for diabetic foot osteomyelitis

Surgical	Medical
Advantages	
Removes necrotic bone*	Avoids surgical procedure
Removes bacteria and biofilm*	Potentially avoids hospitalization
Removes bony prominences*	Preserves more of foot
Opportunity to stabilize foot	May shorten duration of hospitalization
Disadvantages	
May increase risk of reulceration	Increases risk of infection recurrence
Expensive	Risk of reulceration if uncorrected foot deformity
Risk of operative morbidity	Antibiotic-related toxicities
May destabilize foot	Risk of developing antibiotic resistance
Risk of transfer ulcers	Risk of <i>Clostridium difficile</i> disease

Exceptions to each of these items may apply in individual cases or in specific health care settings. *May only be partial or temporary.

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See accompanying article, p. 789.

Table 2—Factors potentially favoring selecting either primarily medical or primarily surgical treatment for diabetic foot osteomyelitis**Medical**

Patient is too medically unstable for surgery
 Poor postoperative mechanics of foot is likely (e.g., with mid- or hindfoot infections)
 No other surgical procedures on foot are needed
 Infection is confined to small, forefoot lesion
 No adequately skilled surgeon is available
 Surgery costs are prohibitive for the patient
 Patient has strong preference to avoid surgery

Surgical

Foot infection is associated with substantial bone necrosis
 Foot appears to be functionally nonsalvageable
 Patient was already nonambulatory
 Patient is at particularly high risk for antibiotic-related problems
 Infecting pathogen is resistant to available antibiotics
 Limb has uncorrectable ischemia (precluding systemic antibiotic delivery)
 Patient has strong preference for surgical treatment

(20), while those of the Infectious Diseases Society of America state “clinicians can consider using either primarily surgical or primarily medical strategies for treating diabetic foot osteomyelitis in properly selected patients” (1). Thus, which approach to take is a question in true equipoise. Now, thankfully, there are new data upon which to make a choice.

In this issue, Lázaro-Martínez et al. (21) present the results of a randomized comparative trial of initial medical versus surgical treatment for diabetic foot osteomyelitis. It is commendable that they conducted such a study at all, as the design presents substantial problems, especially with ethical considerations and ensuring a uniform a surgical approach. In this single-site study, one highly experienced foot surgeon performed all of the surgical procedures. The primary outcome they selected was the rate and time until “healing” (complete epithelialization) of the ulcer or operative wound in those undergoing surgery. They compared the 24 evaluable patients in the antibiotic group and the 22 in the surgical group and noted rates of healing (75.0 vs. 86.3%, respectively) and time to healing (7 vs. 6 weeks, respectively) were not significantly different. There were also no significant differences in rates of adverse events or need for posttreatment surgery in the two groups.

Strengths of this study include the fact that they discontinued antibiotic therapy for 2 weeks before randomizing

patients, obtained deep-tissue specimens for culture, and modified their antibiotic therapy according to the culture results. The patients’ foot lesions were appropriately evaluated, the patients received proper wound care, and the investigators measured serum inflammatory markers at enrollment and after healing.

This study also has several limitations, some of which are substantial. While osteomyelitis was diagnosed by a validated combination of plain radiographs plus the probe-to-bone test (22), the criterion standard for this diagnosis is still bone culture and histology. Bone specimens were cultured from the patients who underwent surgery, but the results are only provided by bacterial species, not by patient. Further, the investigators excluded patients with severe infections, peripheral arterial disease, poor glycemic control, and several common morbidities. It is not surprising, therefore, that among 156 patients evaluated only one-third were eligible for inclusion. This not only limits the generalizability of the study but also left a relatively small study population (52 patients). Thus, the finding of no statistically significant difference between the medically and surgically treated patients is subject to the possibility of missing a true difference (a type 2 error). In addition, although patients with infections of all parts of the foot were eligible, only those with forefoot osteomyelitis wound up

meeting enrollment criteria. Therefore, these results apply to only a minority of patients with diabetic foot osteomyelitis.

Another issue of note is that all of the patients in the surgical group had had systemic antibiotic therapy (of variable duration) up to 2 weeks prior to the randomization and for 10 days after surgery. Thus, we should properly consider this arm of the trial as “primarily” surgical therapy. The duration of therapy selected for the antibiotic-treated patients was 90 days, unless healing occurred sooner.

Unfortunately, there are limited data upon which to decide how long to treat chronic osteomyelitis (23); while 4–6 weeks (or even less) may be sufficient, in published case series patients were generally treated for ≥ 3 months, as in the current study. A further concern is that all enrolled patients were followed up for only 12 weeks after treatment. Some data suggest that most recurrences will occur within this period (24), but many experts would argue for a minimum of 1 year of follow-up to ensure the cure of osteomyelitis (1,7).

An additional concern is that the main end point in this study was “healing” (meaning of the overlying soft-tissue wound), with need for surgery or ulcer recurrence serving as secondary end points. Ideally, we would like to know that infection of the bone was truly eradicated, although ensuring this by bone culture would not be practical. It is reassuring that serum inflammatory markers dropped in most patients who were considered healed, but it would have been even more compelling if follow-up imaging tests further confirmed resolution of bone infection. Finally, the primary analysis in this study should have been on the intention-to-treat population, rather than those who were left after six enrolled and randomized subjects dropped out. Doing so would give a healing rate of 72.0% for the antibiotic group and 70.4% for the group, emphasizing the similarity in outcomes.

So, have we answered the question as to whether primarily medical or surgical therapy is best for diabetic foot osteomyelitis? These data,

notwithstanding their flaws, certainly support those from previous retrospective studies in demonstrating that antibiotic therapy alone can be curative. But it is key to select the proper patients if one elects to go this route: those without severe or necrotizing soft-tissue infections or peripheral arterial disease and perhaps only those with forefoot involvement. Among the remaining issues to address in treating diabetic foot osteomyelitis are better defining the subgroup of patients for whom surgery may be unnecessary and determining the optimal duration and route of antibiotic therapy. The study by Lázaro-Martínez et al. (21) represents more than a “small step,” but a larger investigation that avoids the deficiencies in this one will be needed to make a “giant leap.”

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