Diabetic foot osteomyelitis treatment: an audit of success rates in differing circumstances

Hannah Bond, Lisa Metcalf, Ravikanth Gouni and Susan Snape

Osteomyelitis is a common complication of diabetic foot infection and is associated with a high burden of morbidity and mortality. The success rates of treatment for diabetic foot osteomyelitis treated both surgically and conservatively with antibiotics are widely documented. This study aimed primarily to establish clinical outcomes for people treated with intravenous antibiotics for diabetic foot osteomyelitis at an acute hospital in the UK. The study's secondary aim was to examine these outcomes in the presence of a variety of factors, including location of osteomyelitis, the presence of peripheral arterial disease, previous treatment with oral antibiotics and the results of microbiological sampling.

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Key words

- Osteomyelitis
- Intravenous antibiotic treatment
- Prognosis
- Associated factors
- Microbiology

Osteomyelitis is associated with a high burden of morbidity and mortality (Lavery et al, 2006; Lipsky et al, 2006; Raspovic and Wukich, 2014). Recent guidance recommends the consideration of antibiotic therapy alone in cases of uncomplicated forefoot osteomyelitis with no other indications for surgery (International Working Group on the Diabetic Foot [IWDGF], 2019) and it is preferable to use oral agents in these cases (Aragón-Sánchez and Lipsky, 2018). The IWDGF (2019) guidelines also state that hospital admission for parenteral antibiotics and consideration of surgical intervention should be arranged for cases of severe infection or those unresponsive to oral agents.

Various factors may have a negative impact on outcomes for people with diabetic foot ulcers and infection. The presence of peripheral arterial disease (PAD) is associated with poorer outcomes (Beckert et al, 2006; Ince et al, 2007; Prompers et al, 2008) as is the location of osteomyelitis, with mid- or hindfoot having a poorer prognosis than forefoot disease (Aragón-Sánchez et al, 2008; Arias et al, 2019). Targeted antibiotic treatment based on bone cultures results in better outcomes than empirical treatment (Senneville et al, 2008); however, little literature has examined outcomes associated with the specific organism cultured. Tice et al (2003) demonstrated a two-fold greater recurrence of osteomyelitis when *Pseudomonas aeruginosa* was found on wound culture when compared to *Staphylococcus aureus*, but this study did not focus specifically on diabetic foot osteomyelitis (DFOM). Fewer articles consider the impact these factors might have in cases of DFOM severe enough to require longer-term intravenous (IV) antibiotic treatment; more studies focus on outcomes following oral therapies (Spellberg and Lipsky, 2012).

The Specialist Multidisciplinary Foot Service at Nottingham University Hospitals NHS Trust (NUH) provides both in- and outpatient care. In 2015 and 2016, over 1,000 new referral and over 10,000 follow-up appointments were made at the outpatient clinic. During this time, 266 people were treated for DFOM with oral antibiotics for a period of 6–10 weeks. Of these, 61.7% achieved clinical resolution of their osteomyelitis with no further treatment. This is a similar figure to other published studies (Game and Jeffcoate, 2008; Senneville et al, 2008). People whose osteomyelitis failed to resolve with oral treatment or those with severe infection were admitted to hospital and were usually commenced on IV antibiotic treatment. Surgical interventions were made where necessary.

Aim

The aim of this study was to determine the treatment outcomes of people treated for DFOM

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Article points

1. This study aimed to determine the outcomes of treating diabetic foot osteomyelitis with intravenous antibiotics and examine clinical outcomes in the presence of a variety of factors.
2. Success rates of treatment for diabetic foot osteomyelitis varied substantially depending on the situation.
3. There was a considerable change in the spectrum of bacteria grown following the first course of intravenous treatment in people who had subsequent samples taken.
4. The audit findings will be used to give patients a more detailed prognosis based on their individual circumstances.

Table 1. Surgical procedures performed prior to the initiation of intravenous antibiotics (*n*=119).

Procedure	Total number (%)
Wound debridement alone	41 (34.4)
Wound debridement with local antibiotics ($CaSO_4$ plus gentamycin and/or vancomycin)	51 (42.9)
Digit amputation	7 (5.9)
Digit amputation with local antibiotics	18 (15.1)
Forefoot amputation	2 (1.7)
Surgery	**Total number (%)**
With local antibiotics	69 (58)
Without local antibiotics	50 (42)

with IV antibiotics at NUH during 2015 and 2016 and examine the relationship between the aforementioned factors and clinical outcomes. The primary outcome measure in this study was whether the initial DFOM was considered clinically resolved 12 months after the initiation of IV therapy without any further surgery, IV antibiotics or amputation. Overall healing rates of any associated wounds at 12 months were also measured. Secondly, these outcomes were examined with regards to the anatomical location of the DFOM, the presence of PAD, previous treatment with oral antibiotics and the results of microbiological sampling.

Methods

The study population were identified retrospectively via two different databases: The Diabetic Foot Ward admissions and Outpatient Parenteral Antimicrobial Therapy databases for the study period were examined. The record of every person on these lists was accessed and those being treated specifically for DFOM was determined from both. Outpatient Parenteral Antimicrobial Therapy services in Nottingham offer self-administration, daily appointments at the infusion centre, or home visits for those who are housebound or require multiple daily doses of antibiotics. People were excluded if they had received IV treatment for a related DFOM outside the study period or had soft tissue infections without recorded evidence of DFOM.

Hospital notes, letters and photos along with radiological investigations were used to assess the outcome measures at 12 months. Resolution of DFOM was defined as no noted clinical signs of infection at the initial or a contiguous site. The presence of PAD was determined by clinical assessment and duplex scan results.

Study population

In total, 145 people were identified as having completed IV treatment for DFOM. Six were lost to follow up, resulting in a study population of 139. The population had a mean age of 64 years (range: 30–92 years) and a mean HbA_{1c} of 77 mmol/mol (range: 43–122 mmol/mol). The majority (74%) were male, 84% had type 2 diabetes and 84% had received a diagnosis of diabetes over 10 years prior to the study period.

The choice of antibiotic was determined on an individual basis under advisement from a consultant microbiologist. The duration of treatment was 6–12 weeks. People remained under the care of the multidisciplinary foot service and received ongoing wound debridement, offloading and vascular interventions where appropriate.

Initial surgery

Of the study population, 85.6% had initial therapeutic surgery (*Table 1*). Those who had diagnostic bone biopsies only were excluded. Over half of initial surgeries involved the insertion of highly purified calcium sulfate impregnated with antibiotics. Most people who did not have localised antibiotics required topical negative pressure therapy.

Results

Osteomyelitis resolution and wound healing

Table 2 shows therapeutic success and wound healing rates at 12 months. After 1 course of IV therapy, 63.3% of DFOM resolved clinically without the need for further IV therapy or surgery. A second course of IV therapy was given to 32 people, with 43.8% resolution, and three courses to eight people, with 37.5% resolution. Cumulatively, 75.6% of cases were successfully resolved 12 months after IV antibiotic initiation, regardless of how many courses were required.

At 12 months, half of the wounds had healed, an additional 8% had healed following amputation and 27% were ongoing. Fifteen per cent of people were deceased 1 year after treatment.

Location of osteomyelitis

The location and resolution of osteomyelitis

are given in *Figure 1*. The majority of people were treated for DFOM affecting the forefoot. Fifteen out of 16 people with digital DFOM achieved clinical resolution without any further intervention. Resolution rates were significantly lower for DFOM of the fore-, hind- and midfoot.

Peripheral arterial disease status

Just over half (54%) of people were deemed to have PAD. At 12 months, 58.7% of these individuals had achieved clinical resolution of DFOM (*Figure 2*). Of people without PAD, 68.8% of DFOM cases were resolved.

Prior treatment with oral antibiotics

Previous oral antibiotics — defined as the use of oral antibiotics for this episode of DFOM within the 12 weeks prior to commencing IV therapy — had been given to 28.8% of people. A further 29.5% of individuals had received antibiotics for soft tissue infection but subsequently developed DFOM. The remainder had not received oral antibiotics. Clinical resolution was greater in antibiotic-naive people than in those who had received prior oral antibiotics for soft tissue infection or for DFOM (*Figure 3*).

Organisms isolated in samples

Antibiotic choice was guided by culture from samples of bone (*n*=86), tissue (*n*=35) or wound aspirate (*n*=6). Three samples showed no growth. No samples were taken from six individuals.

Table 2. Therapeutic success and wound healing rates of people after receiving one course of intravenous antibiotics for diabetic foot osteomyelitis (*n*=139).

Variable	Total number	Therapeutic success at 12 months (%)	Healed wounds in surviving patients at 12 months (%)
Location of osteomyelitis			
Digit	16	15 (93.8)	11 (78.6)
Forefoot	78	50 (64.1)	45 (66.2)
Midfoot	20	9 (45.0)	8 (42.1)
Hindfoot	25	15 (56.0)	6 (35.3)
Peripheral arterial disease status			
Present	75	44 (58.7)	31 (47.0)
Absent	64	44 (68.8)	39 (75.0)
Prior oral treatment for infection			
For osteomyelitis	40	19 (47.5)	22 (61.1)
Soft tissue infection only	41	26 (63.4)	16 (48.5)
None	58	43 (74.1)	32 (65.3)
Isolation of organisms			
Single	43	27 (62.8)	21 (53.8)
Multiple	87	56 (64.4)	44 (62.9)
No growth	3	0 (0.0)	0 (0.0)
No sample taken	6	5 (83.3)	5 (83.3)
Cultured organisms			
Gram-positive	61	46 (75.4)	35 (66.0)
Gram-negative	18	7 (38.9)	7 (41.2)
Gram-positive and -negative	41	25 (61.0)	17 (36.7)
Anaerobes (in isolation or combination)	10	5 (50.0)	6 (66.7)
Total	**139**	**88 (63.3)**	**70 (64.8)**

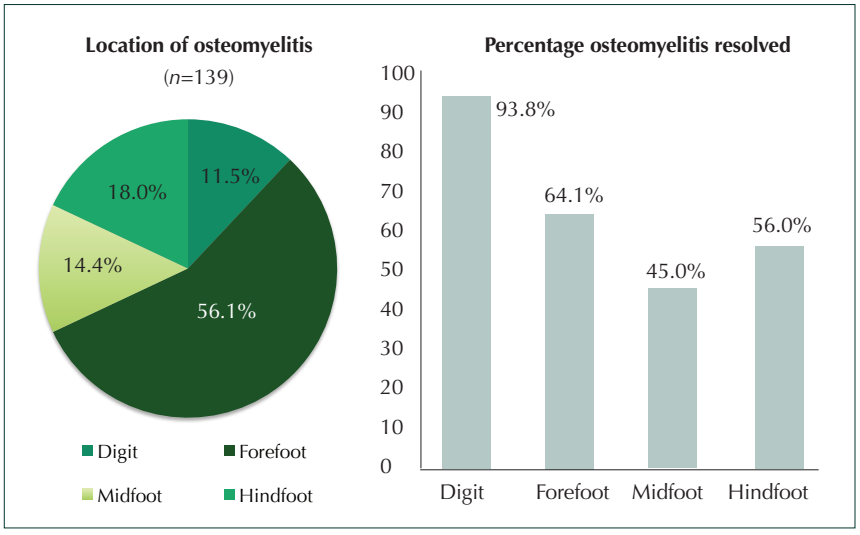

Figure 1. Osteomyelitis location and resoluton at 12 months following one treatment course.

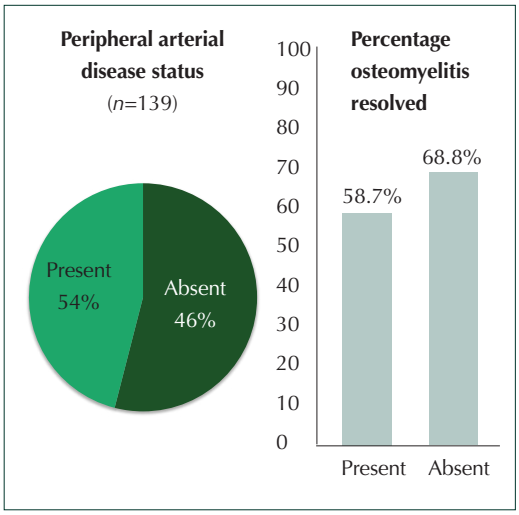

Figure 2. Peripheral arterial disease status and its impact on osteomyelitis resolution at 12 months.

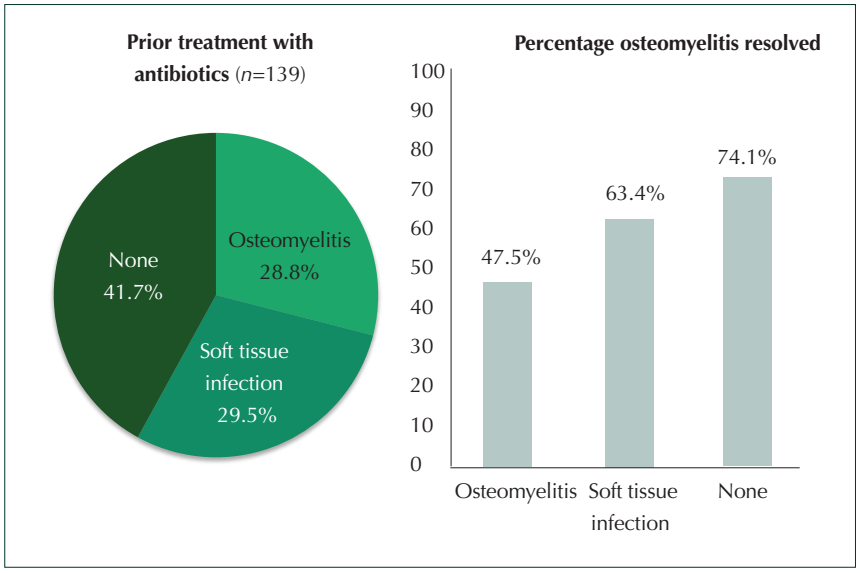

Figure 3. Reasons for prior antibiotic treatment (left) and resolution of osteomyelitis at a year.

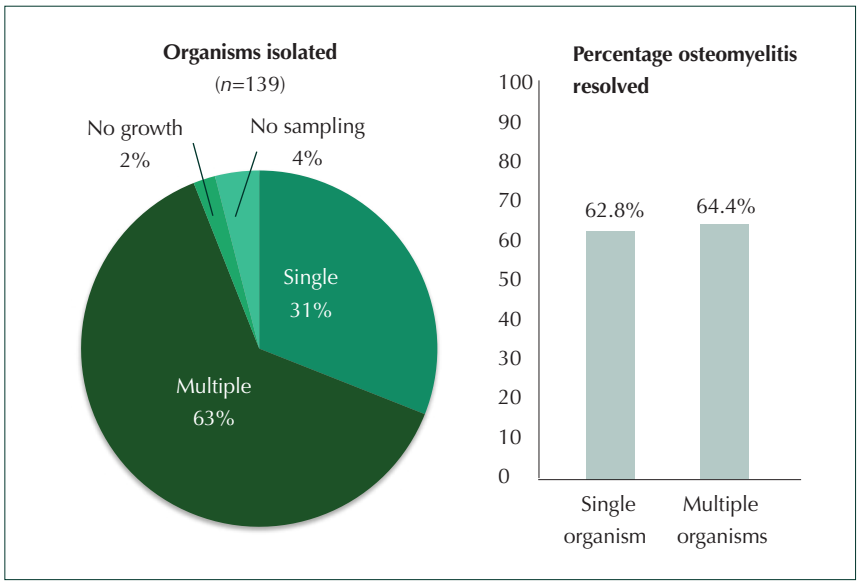

Figure 4. Organisms isolated and resolution of osteomyelitis after one course of treatment.

Almost two-thirds of samples cultured more than one organism (*Figure 4*). There was little difference in clinical resolution between those who cultured single and multiple organisms.

Of the samples cultured, 46.9% contained Gram-positive organisms only; this group had the highest rate of clinical resolution (*Figure 5*). DFOM resolved in 61% of people whose samples grew both Gram-positive and -negative organisms on culture. Half of the samples that grew anaerobes resolved. Individuals whose samples grew only Gram-negative organisms had the lowest rate of resolution (38.9%) at 12 months.

Microbiology

There were 40 instances of repeat IV treatment and the organisms grown from subsequent samples were examined. Additional organisms grew in 18% of cases, with entirely different organisms being present in 60% of cases. Twenty-eight different organisms were identified from sampling.

Discussion

Osteomyelitis was successfully treated with one course of IV antibiotic treatment in 63.3% of people. The overall 12-month resolution rate was 75.6%. This is similar to other published studies, which report resolution rates of between 60% and 80% (Game, 2010). The percentage of people treated with IV antibiotics who achieved clinical resolution of DFOM after one course of treatment was very similar to that of people who had received oral antibiotic treatment. Over 40% of people had not previously received oral antibiotics. The reasons for first-line treatment with IV antibiotics were examined in order to establish whether people were being treated with IV antibiotics when oral antibiotics could have been considered. There was clear clinical justification in all cases. Most people were systemically unwell or had rapidly deteriorating wounds or samples had cultured organisms sensitive only to antibiotics that required IV delivery.

Overall, the best outcomes were observed in people who were treated for forefoot or digital osteomyelitis, did not have PAD, had received no prior antibiotic treatment and whose samples grew Gram-positive organisms only or a mix of Gram-positive and Gram-negative organisms. In these 26 individuals, DFOM resolved with no further treatment in 92.3% of cases. The poorest outcomes were in people with a combination of PAD, previous oral treatment for DFOM and Gram-negative organisms on culture. In this group of 17 people, 58.8% required further treatment. Due to the study population size, this includes people who had DFOM at any site. Osteomyelitis did not resolve in the two people with midfoot or hindfoot DFOM.

The outcome of treatment for DFOM with IV antibiotics varied in this study population. It was expected that people with hindfoot DFOM or PAD would have lower resolution rates but the presence of Gram-negative bacteria and previous treatment with oral antibiotics appears to suggest a reduced chance

of clinical resolution. This is not suggesting that the use of oral antibiotics in itself decreases the success rate of IV therapy but there is a possibility that more resistant organisms are selected out by the use of any antibiotic therapy.

There was a change in the spectrum of bacteria grown following the first course of IV treatment in people who had subsequent samples taken. This could suggest that the antibiotics largely eliminated the original pathogen but infection continued due to the proliferation of others. Whatever the cause, it appears that repeat biopsy for microbiology is necessary if infection is not responding to treatment.

The population size in this audit was too small to reliably establish whether or not the factors studied had a significant relationship with DFOM resolution. This audit has, however, provided a better understanding of the outcomes at NUH and has already been used to give more specific advice on prognosis based on people's individual circumstances.

Conclusion

Clinical resolution rates of DFOM with IV and oral antibiotics were similar in this study, however, the use of IV antibiotics was justified in all cases. Forefoot and digital DFOM were more likely to respond to IV antibiotics than mid- or hindfoot DFOM. PAD may have had a negative impact on outcomes. The type of organism(s) present affected resolution rates and pathogens cultured from repeat samples often differed from the initial culture. The results of this audit are being used to inform prognosis at NUH. ■

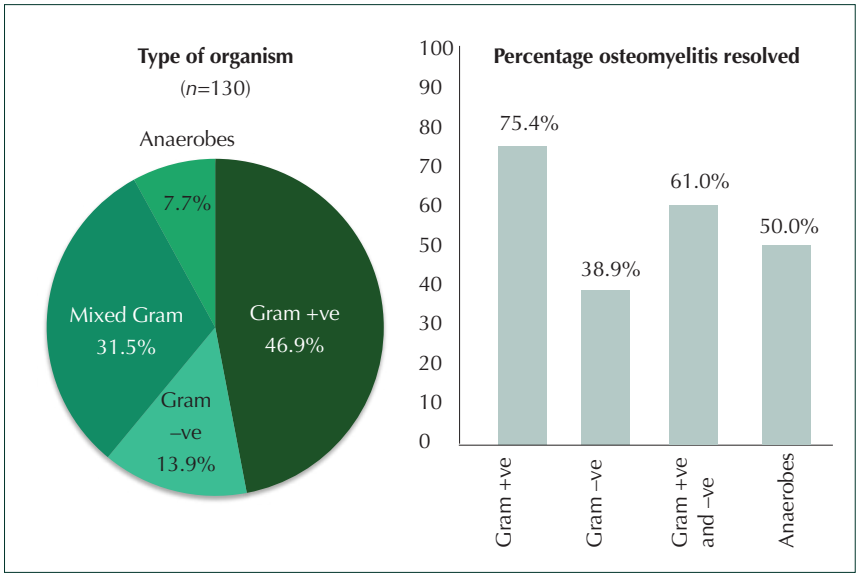

Figure 5. Type of organism and resolution of osteomyelitis after one course of treatment.

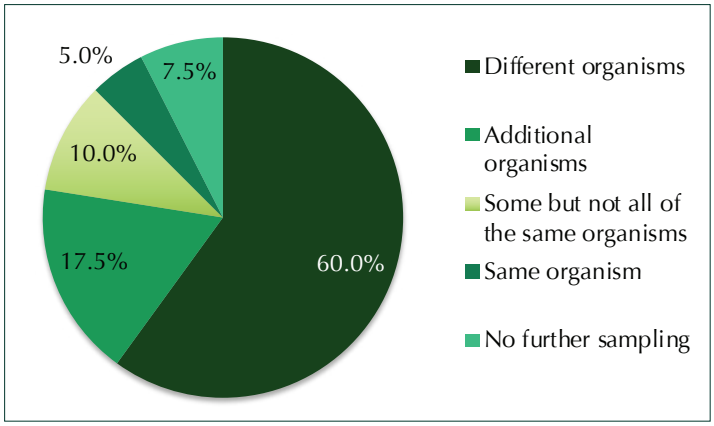

Figure 6. Microbiology for repeated intravenous antibiotics treatment (n=40).

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