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Diabetic calcaneal osteomyelitis

Felix W.A. Waibel[1], Ilker Uçkay[2,3], Kati Sairanen[2], Lorenz Waibel[4], Martin C. Berli[1], Thomas Böni[1], Karim Gariani[5], Benjamin A. Lipsky[6]

[1]Department of Orthopedic Surgery, Balgrist University Hospital, Zurich, Switzerland;
[2]Unit for Clinical and Applied Research, Balgrist University Hospital, Zurich, Switzerland;
[3]Infectiology, Balgrist University Hospital, Zurich, Switzerland;
[4]Department of Radiology, University Hospital Freiburg, Germany;
[5]Service of Diabetology and Endocrinology, Geneva University Hospitals, Switzerland;
[6]Department of Medicine, University of Washington, Seattle, USA

SUMMARY

Diabetic foot infection (DFI), a multi-facetted disease requiring a multidisciplinary approach for successful treatment, mostly affects the forefoot. Calcaneal osteomyelitis (CO) is an uncommon presentation of DFI with a somewhat different epidemiology, clinical features, and approach to management. These patients, compared to those with non-calcaneal DFI, more often require special surgical techniques and off-loading approaches. In this narrative review targeted to non-surgical clinicians, we explore how CO differs from other types of DFI affecting other anatomical locations. Based on our review of the literature and personal experience, we also highlight important issues regarding the management of CO osteomyelitis, including the need for specialized surgical approaches.

Keywords: diabetic foot osteomyelitis, calcaneus, epidemiology, management, outcomes.

INTRODUCTION

Infections of the foot in persons with diabetes are an increasingly common problem that is often associated with substantial morbidity, including lower extremity amputation [1]. While these diabetic foot infections (DFI) can affect any anatomic site, the calcaneus is involved in only 7-8% [2]. In those patients with Charcot arthropathy, 27% of cases complicated by osteomyelitis occur in the calcaneus [3]. Clinical experience suggests that calcaneal osteomyelitis (CO) may be most likely to occur in immobile patients (with posterior heel ulcerations and decubitus) who have a major gait disorder and are elderly [4]. It is likely that there are other differences between diabetic patients with calcaneal osteomyelitis compared to non-calcaneal DFI. In addition, the surgical approach to calcaneal osteomyelitis may be more challenging than for forefoot infection, as the calcaneus is subject to axial loading during heel strike and transfers load to the midfoot during the push-off process [5]. Furthermore, pressure off-loading may be more difficult for CO than other anatomic areas, and arterial perfusion is provided only by the peroneal and posterior tibial arteries [6]. Thus, it is not surprising that even with optimized management, secondary amputations after initial calcanectomy are required in up to 67% of the cases, including major amputations in half the cases [7-14].

In light of the fact that calcaneal osteomyelitis is relatively uncommon, and clinicians may be unfamiliar with the specific features important in properly caring for this infection, we reviewed our extensive experience with musculoskeletal infection. We herein provide a narrative mini-review of our single-center experience and compare our data to that gleaned from a literature review on the epidemiology, diagnosis, treatment modalities, pitfalls and outcomes of CO compared to non-calcaneal DFI.

Corresponding author
Ilker Uçkay
E-mail: ilker.uckay@balgrist.ch

METHODS

We used the data from a 2018 paper, which contains the largest known published single-center database on DFI that contained data on clinical follow-up of at least two years after the inclusion of the last patients (Table 1) [15]. The authors, an international team of orthopedic surgeons, infectious diseases physicians, a radiologist, a study nurse and a diabetologist with experience in DFI and related research, reviewed the medical records to find and compare data from cases of diabetic CO and non-calcaneal DFI. We then completed this comparison with a Cox regression analysis

Table 1 - Comparison of patients presenting with diabetic calcaneal infection with those presenting with non-calcaneal diabetic foot infections.

n = 721	*Diabetic calcaneal infection*	*p value**	*Non-calcaneal diabetic foot infection*
	n = 59		*n = 662*
Female sex	15 (24%)	0.52	205 (28%)
Age (median)	65 years	0.14	69 years
Transcutaneous oxygen level foot (median)	36 mm Hg	0.06	30 mm Hg
Past history of stroke	2 (4%)	0.29	46 (7%)
Ischemic cardiopathy	20 (34%)	0.77	237 (36%)
Retinopathy	30 (51%)	0.06	253 (38%)
Glycosylated serum hemoglobulin level (median)	7.5%	0.98	7.4%
Diabetes type 1	11 (19%)	***0.03***	49 (4%)
Duration of diabetes (median)	21 years	***0.01***	15 years
Insulin therapy	43 (73%)	0.28	437 (66%)
Additional (non-diabetic) immune suppression*	3 (5%)	0.52	23 (4%)
Bacteremic infection	0 (0%)	***0.01***	68 (10%)
Polymicrobial infection	33 (53%)	0.09	308 (42%)
- Mostly due to *S. aureus*	27 (44%)	0.96	316 (43%)
- Mostly due to streptococci	8 (13%)	0.51	118 (16%)
Enterococcal involvement	10 (16%)	0.18	77 (11%)
- Mostly Gram-negatives	35 (56%)	***0.01***	242 (33%)
Mostly due to *P. aeruginosa*	12 (20%)	***0.01***	37 (6%)
Presence of a soft tissue abscess	20 (34%)	0.29	182 (28%)
Number of surgical interventions (median)	1	0.34	1
- (Partial) amputation	20 (32%)	***0.01***	418 (57%)
Negative-pressure vacuum therapy throughout	20 (34%)	***0.01***	76 (11%)
Duration of antibiotic treatment (median)	33 days	0.09	30 days
> 21 days of total antibiotics	43 (69%)	0.54	477 (65%)
Duration of intravenous treatment (median)	5 days	0.64	5 days
Clinical revascularization	181 (29%)	0.92	53 (30%)
Length of hospital stay (median)	25 days	0.89	28 days
Overall treatment failure	19 (32%)	0.16	159 (24%)

Significant p values ≤ .05 (two-tailed) are displayed ***in bold and italic***. Pearson-$\chi 2$ and Wilcoxon-ranksum-tests, as appropriate.
* Immune-suppression beyond that of diabetes mellitus = active cancer, dialysis, cirrhosis CHILD C, untreated HIV disease and immunosuppressive drugs > equivalent of 15 mg prednisolone.
S. aureus = Staphylococcus aureus; P. aeruginosa = Pseudomonas aeruginosa.

Table 2 - Regression analysis with outcome "treatment failure" comparing diabetic patients with calcaneal osteomyelitis versus diabetic patients with non-calcaneal foot infections (*hazard ratios with 95% confidence intervals*). Adapted from Reference 15.

	Univariate results	*Multivariate results*
Female sex	1.0, 1.0-1.0	0.8, 0.4-1.3
Age > 60 years	1.1, 0-6-1.9	n.d.
Transcutaneous oxygen level foot (*continuous variable*)	1.0, 1.0-1.0	1.0, 1.0-1.0
Bacteraemia	0.5, 0.2-1.1	n.d.
Number of past episodes of diabetic foot infection	1.0, 0.9-1.1	0.9, 0.8-1.1
Past duration of diabetes mellitus (*continuous variable*)	1.0, 1.0-1.0	n.d.
Calcaneal osteomyelitis	1.4, 0.9-2.3	1.3, 0.6-2.8
Number of surgeries	0.9, 0.8-1.1	0.9, 0.7-1.2
Use of vacuum-assistance	***1.1, 1.0-1.1***	n.d.
Duration of total antibiotics (*continuous variable*)	1.0, 1.0-1.0	1.1, 0.6-1.5
Duration of parenteral antibiotics (*continuous variable*)	1.0, 1.0-1.0	n.d.
Revascularisation	1.0, 0.7-1.4	n.d.

Significant results are displayed ***in bold and italic***. n.d. = not done

adjusting for the outcome "treatment failure" to determine the role of a calcaneal osteitis involvement in the overall remission in DFIs (Table 2). In a second step, we performed a narrative scientific literature search using:

1) the following English MeSH terms: "heel", "calcaneus", "diabetes", "infection" and/or "osteomyelitis"; and,
2) the corresponding words in German, French, Finnish, and Turkish languages. From our search of PubMed, Google (Scholar) and any additional references from the retrieved articles, we appraised 82 papers.

From these we excluded 45 papers for the following because they: were reviews without their own cases (n=12); had insufficient data (n=15); included uninfected calcaneal ulcers (n=4); had redundant data (n=4); and, were missing information regarding the patients' diabetes status (n=10). Thus, we summarized 37 papers in Table 3, from which we synthetized our review.

SYNTHESIS OF THE REVIEW

Pathogenesis

Based on the available literature, the main reasons for development of CO after open fractures and surgical site infections after calcaneal surgery in the diabetic foot are the presence of a chronic ischemic pressure ulcer or a neglected decubitus in a bedridden patient [2, 4, 12, 16, 18]. The presence of diabetic neuropathy significantly enhances the risk of these complications [19, 20]. Indeed, the loss of protective sensation, dryness of the skin with subsequent callus formation and reduction of the size of the heel fat pad each add to the risk of an unrecognized elevated plantar peak pressure on the heel [21-23]. The absence of bacteremia in CO cases (Table 1) underlines its local (rather than hematogenous) origin by contiguous spread from a soft tissue infection, often with a persistently draining sinus tract. In contrast, structural deformations or non-adapted footwear are not underlying causes of CO, as they often are in cases of toe DFIs, including toe osteomyelitis [24]. Iatrogenic inoculations of organisms during steroid injections for plantar fasciitis are a rare cause of CO. In both the literature and in our database analysis, we do not know how many heel ulcers were initiated by significant trauma. Thus, most calcaneal ulcers are not related to a remarkable origin that the patients could recall.

Epidemiological associations and pathogens associated with diabetic calcaneal osteomyelitis

There is a paucity of studies investigating the epidemiological and specific risks factors associated with CO in persons with diabetes. Based on data from our cohort in Geneva University Hospitals,

Table 3 - Summary of the published literature on patients with diabetic calcaneal osteomyelitis.

First author	*Year*	*No. of patients*	*No, with diabetes*	Pathogens *in bone*	*Total antibiotic duration (days)*	*Remission in %*	*Minimal follow-up (month)*
Crandall [9]	1981	*31*	*18*	*Proteus, E. coli,* Enterococci	*n.a.*	*45.1*	*120*
Wang [2]	1992	52	0	*P. aeruginosa,* MSSA, *S. pyogenes*	n.a.	100	111
Smith [67]	1992	12	7	*n.a.*	n.a.	71	12
Baumhauer [8]	1998	8	6	*n.a.*	n.a.	100	27.3
Laughlin [29]	1999	47	21	MSSA, MRSE, Streptococci	36	52	n.a.
Baravarian [26]	1999	12	12	MSSA, *P. aeruginosa, B. fragilis*	42	83	13
Bollinger [58]	2002	22	9	*n.a.*	n.a.	81.1	27
Chen [27]	2005	11	11	MSSA, *S. epidermidis*	35	100	6
Flieger [76]	2006	70	n.a.	MSSA, *S. epidermidis, S. capitis,* Streptococci	47	n.a.	76.8
Kurvin [77]	2009	23	21	MSSA	n.a.	n.a.	n.a.
Ignatiadis [73]	2011	6	5	*n.a.*	n.a.	100	18
Goudie [66]	2012	21	21	*n.a.*	n.a.	57	24
Ghods [78]	2012	3	0	*E. coli,* Streptococci, MSSA, *S. epidermidis*	n.a.	33	19
Wronka [18]	2012	1	1	MSSA	n.a.	100	n.a.
Bibbo [31]	2012	1	1	*S. epidermidis*	56	100	12
Van Riet [11]	2012	24	7	*n.a.*	n.a.	87.5	37
Walsh [13]	2013	10	7	MRSA, MSSA, *P. aeruginosa*	n.a.	90	n.a.
Shojaiefard [20]	2013	12	12	*n.a.*	42	89	12
Faglia [14]	2013	17	17	MSSA, MRSA, Streptococci, *P. aeruginosa*	35	65	n.a.
Boffeli [79]	2013	3	3	*n.a.*	n.a.	100	9
Schachinger [80]	2014	79	0	MSSA, *E. coli, S. pyogenes, F. magna*	n.a.	n.a.	n.a.
Aragon-Sanchez [81]	2014	52	52	*n.a.*	n.a.	n.a.	n.a.
Iwakura [82]	2014	1	1	*P. mirabilis*	19	100	18
Oliver [69]	2015	42	35	*n.a.*	n.a.	71	41
Lin [89]	2015	1	1	MSSA	28	100	12
Jiang [32]	2015	394	69	MSSA, *P. aeruginosa, E. coli, P. mirabilis*	36	77.74	12
Lesens [24]	2015	74	65	MRSA, MSSA, *P. aeruginosa*	56	80	21
Babamahmoodi [83]	2015	1	1	*Aspergillus ochraceus*	130	100	n.a.
Grecian [84]	2015	8	8	*n.a.*	n.a.	50	6
Memis [85]	2016	1	1	*n.a.*	56	100	n.a.
Evran [86]	2016	4	4	*A. baumannii, K. pneumoniae*	60	n.a.	n.a.
Drampalos [28]	2016	12	12	MSSA, *E. coli, P. aeruginosa*	66	100	4
Allen [87]	2016	1	1	*n.a.*	0	100	12
Dalla Paola [19]	2016	18	18	Enterococci, *P. aeruginosa, MSSA*	28	100	6
Akkurt [88]	2017	23	23	MSSA, *P. aeruginosa, K. pneumoniae, E. coli*	n.a.	78	3
Mikami [30]	2018	1	1	MSSA, *Bacteroides*	21	100	24
Waibel [12]	2019	50	36	MSSA, Enterococci, *E. cloacae*	42	50	6

MSSA = Methicillin-sensitive *S. aureus*; MRSA = Methicillin-resistant *S. aureus*.

CO patients do not differ from those with other types of DFI in sex distribution, age, percentage on insulin therapy, past glycemic control, history of stroke, need for lower extremity revascularization, or myocardial infections. They do, however, have a history of a longer duration of diabetes and are more often diagnosed with diabetes mellitus type 1 and probably with retinopathy (Table 1). CO is also more often a polymicrobial infection (Table 1) compared to the forefoot DFO [1, 19, 24, 25]. Although the most common pathogens isolated from patients with CO are *Staphylococcus aureus*, *S. epidermidis*, *Proteus mirabilis*, and *Enterococcus*, they are statistically and significantly more likely to have infections with Gram-negative bacteria such as *Bacteroides*, *Pseudomonas aeruginosa* or *Escherichia coli* [1, 9, 13, 19, 26-32] (Table 1). These microbiological findings may be related to the frequent presence of chronically macerated skin, rather than a dry pressure ulcer typically seen in forefoot DFUs. Laughlin et al. found an average of 4.2 pathogens among CO cases (soft tissue and bone), while Walsh et al. reported an average of 4.4 pathogens [13, 29].

Clinical and microbiological diagnosis

DFI classification systems such as the Wagner, PEDIS or the University of Texas classification are useful for categorizing the severity of DFI and may help in their management and prediction of treatment outcomes [33, 34]. The localization of a DFI (*e.g.*, plantar versus dorsal or heel) is important in determining the type of pressure off-loading required. The presence of visible or palpable (via the probe-to-bone test) bone is highly suggestive, but not definitive proof, of osteomyelitis [24]. The best way to confirm the presence of diabetic foot osteomyelitis (DFO), as well as to get information on the causative pathogens and their antibiotic susceptibility remains obtaining a bone specimen by biopsy or from intraoperative specimens [35]. Bone cultures can be falsely-negative related to sampling errors or recent treatment with antibiotics. Similarly, they can be falsely-positive due to specimen contamination. Performing histopathological examination of a bone specimen can be useful in patients on antibiotic therapy; however, they can also be falsely negative due to sampling error or falsely-positive when the patient has a non-infectious inflammatory disorder [35].

Imaging diagnosis

There are a variety of imaging tests for assessing bone infections. We found no specific approaches that are different for managing CO compared with non-calcaneal DFI. For both DFI and CO, plain radiography is usually the first (and often only) imaging method, as it is widely accessible, relatively inexpensive and can be interpreted by most clinicians. Unfortunately, plain X-rays are often normal in the early stages (first few weeks) of diabetic foot osteomyelitis, including CO [36]. One meta-analysis in patients with DFI found a pooled sensitivity of 0.54 and specificity of 0.68 [37]. Characteristic findings of osteomyelitis in plain radiographs includes focal bony lysis or cortical loss, periostal reaction or elevation, formation of new bone and regional osteopenia or trabecular pattern [35, 38-40]. Soft tissue swelling may be an early sign for osteomyelitis but is not specific [41]. Radiological signs that are largely pathognomonic include the presence a sequestrum, involucrum or cloaca [42]. Despite its shortcomings, plain radiography remains the first-line imaging technique even in clinically clear CO, as it can help to exclude other clinical entities (such as fractures) and to assess the progression of disease [42].

Among advanced imaging techniques, computed tomography (CT) can help resolve anatomically complex situations that remain unclear by plain radiography. It is often indicated in the planning of surgery, *e.g.* for seeking sequestrations, bone destruction, cloacae or to assess the thickness of an involucrum [41]. In addition, using intravenous contrast administration can help detect soft tissue abscesses, and CT-guidance allows for percutaneous biopsies to obtain material for microbiology [43]. One major disadvantage of CT is that it is associated with a relatively higher radiation exposure than other imaging tests. Compared to magnetic resonance imaging (MRI), its resolution and demonstration of cortical changes are superior, whereas its assessment of soft tissue is inferior, and it cannot reliably demonstrate bone marrow edema [42]. In the future, the dual-energy CT might compensate some current deficiencies, especially for patients with a contraindication to MRI, as it would display bone marrow edema [44, 45]. MRI is particularly helpful in detecting bone marrow edema, which is the earliest sign of acute CO, being detected as early as 1 to 2 days after onset of infection [42, 46]. Typical findings

of osteomyelitis on MRI, which may be visible after as little as two days, are loss of focal signal intensity on T1-weighted images, high focal signal on T2-weighted images, and high bone marrow signal in short tau inversion recovery (STIR) sequences [35,47,48]. The MRI has a high sensitivity (93%) and high specificity (79%) for diagnosis of osteomyelitis of the foot [49, 50]. While there are several nuclear medicine techniques available, most are inferior to MRI in CO, with radio-labelled white blood cells being the most accurate [49,51]. While some authorities suggest that in CO it is important to use imaging methods to determine the amount of bone to resect, there are no recommendations on the best approach for this issue. Our recommendation for this determination is to use the extent of loss of focal signal intensity on T1-weighted MR images, as it best reflects the amount of osteomyelitic bone. While there is evidence, that MRI is more precise than radiographs in detecting the extent of osteomyelitis in the forefoot, there is no literature available for CO [52]. We think that routine radiologic follow-up is not necessary when the surgeon is confident that all infected bone has been resected, and a favorable course of therapy is likely. However, repeat imaging is appropriate if CO recurrence is suspected or if the surgical wound has not healed within three months. Clinicians should bear in mind that in the early phase after surgical therapy reactive edema may compromise the validity of a repeat MRI. Therefore, the clinical presentation and the laboratory course are most important in deciding for revision surgery.

Antibiotic therapy

The administration of systemic antimicrobial agents to patients with bone infection is paramount to preventing infection progression and to allow normal wound healing [24,35]. Unless there is total amputation of the infected limb (*e.g.*, a below-the-knee amputation), it is difficult to assess whether or not all infected bone has been removed. This is especially true in the case of a partial calcanectomy for CO, likely even more so than after surgical resection for diabetic toe or metatarsal osteomyelitis.

One way to assess if all infected bone has been removed is to take samples from the residual calcaneal bone after surgical debridement. However, this procedure has several drawbacks. Firstly, the area of resection is usually relatively broad in CO, so that taking a sample from one part does not guarantee there is not residual osteomyelitis even one centimeter away. Secondly, the surgical procedure may contain repetitive debridements, which can cause pathogen transfer onto a previously sterile sample. Obtaining a histologic examination, in addition to a microbiologic one, may therefore be necessary. If histology shows signs of osteomyelitis at the resection border, it is reasonable to assume there is residual bone infection. Pathogen growth in a bone sample, however, could merely represent specimen contamination. Samples of the marginal bone left after surgical resection should generally be taken if the surgeon deliberately leaves a suspicious area of bone because of biomechanical considerations.

Generally speaking, the principles of antibiotic therapy for CO do not differ from those for other DFI localizations. The size and volume of the calcaneal bone does not require a longer duration of treatment or the administration of specific (supposedly bone-penetrating) antibiotic therapy or therapy by the parenteral route. Indeed, the results of our single-center found that the outcomes of the treatment of CO cases are similar to those of other DFI localizations, despite an identical median number of surgical debridements (1 vs. 1 intervention) and median duration of total (33 vs. 30 days) and parenteral (5 vs. 5 days) antibiotic therapy (Table 1). As shown in Table 2, which shows the role of CO in the overall treatment failure for DFI, it does not demonstrate that CO was related to a worse outcome.

Theoretically, initial antibiotic therapy could be administered intravenously, as many clinicians prefer to do, because of the large calcaneus size, but this is not evidence-based. An argument for just oral antibiotic therapy at or soon after the start of treatment is the near-absence of bacteremic infection in CO [15, 24].

Another issue of concern is whether or not to select broad-spectrum empiric antibiotic therapy to preemptively cover against Gram-negative organisms (especially *P. aeruginosa*), as these may be isolated more often than in other DFIs in macerated CO, at least in Western countries (Europe and North America [24, 29]). In the interest of antibiotic stewardship, we advocate against this approach

for non-severe CO cases (without systemic inflammation), as it is likely that waiting for culture results would be safe [24]. Regarding route of antibiotic therapy, patients who are systemically ill will likely benefits from parenteral therapy, which achieves faster and higher serum antibiotic levels [35]. However, oral antibiotic therapy, either after a few days of parenteral treatment or initially for non-severe infections, generally has similar clinical efficacy, fewer complications or lower financial expensive than parenteral therapy [24, 35].

The theoretical advantages of local (topical or implanted) antibiotic therapies for osteomyelitis have been discussed for decades [28, 53]. The relatively abundant calcaneus bone stock would invite this approach, which has been described as the Silo technique (single-stage debridement with absorbable gentamicin-loaded sulphate/hydroxyapatite biocomposite [28]). However, and in contrast to most long bone chronic osteomyelitis cases in human adults, the bone in CO often becomes porous and disintegrates upon relatively minimal force. Moreover, we have found no evidence that combined local and systemic antibiotic therapy is superior to a systemic alone in DFIs, including CO. Implanting calcium sulfate loaded with antibiotics has the potential drawbacks of suboptimal bone formation and the occurrence of pathologic fractures [54-56]. In their review of local antibiotic delivery for DFI, Markakis et al. concluded that "the role of topical antibiotic agents in treating DFI is limited and outside of routine practice" [25]. The duration of antibiotic treatment is largely dependent on the extent of surgical resection of the bone and local soft tissue infection. In moderate infections, one to two weeks of antibiotic therapy is usually sufficient, if all infected bone has been removed [35]. Determining if all osteomyelitis has been resected depends in the first case upon the clinical assessment of the treating surgeon. This may need to be more definitively established by repeated MRIs or bone biopsy for culture if the clinical course suggests residual osteomyelitis. When residual infected bone is suspected or proven, we agree with recommendations of up to six weeks of antibiotic therapy [24, 35, 57]. Of course, clinicians should make efforts for all patients with DFI, including CO, to assess for (and correct if necessary) severe peripheral arterial disease, optimize wound care and glycemic control.

Pressure off-loading and adequate footwear

Off-loading pressure on the affected site until the (surgical) wound has healed and ensuring the patient is provided and routinely uses proper footwear are paramount in both the treatment and prevention of CO [11, 19, 35, 58-61]. However, the type of temporary device is more difficult to choose for calcaneal than for forefoot DFI, given the high-pressure bearing requirement of the hindfoot. Most expert advocate for total contact casting (TCC, Figure 1) and walkers; with targeted ulcer off-loading as the best options to off-load the wound area. There seems no difference in effectiveness between the two devices when used in an irremovable way [60, 62]. The location of the wound cavity is determined by a footprint marking the wound [63]. Based on the available literature, non-removable devices are more effective in healing of (infected) neuropathic calcaneal ulcers than removable devices, because they better ensure the device is used [62, 64]. Concerns about potential adverse effects of non-removable devices, such as secondary ulceration on the affected and non-affected foot, and inconvenience caused by inability to observe and wash the covered site, are not supported in the literature. In two meta-analyses there were no differences in adverse effects between these two types of application [61, 62, 64].

In the author`s practice, costs of a TCC average

Figure 1 - Total contact cast.

about $300 US and that of an off-loading walker about $5000 US. Both devices are theoretically easily accessible: a TCC can be made within 30 minutes when a cast facility is available, while walkers come off the shelf and are available in different sizes. Only the foot bed has to be adapted according to the off-loading needs. Because of the substantially higher costs and the different sizes required, storing a sufficient variety of walkers is difficult, making TCCs are more practical and economical.

We recommend that appropriate professionals see the patient to review both the status of the wound and the effectiveness of the off-loading device at least weekly. If a specialized wound care nurse is available and the clinical course is favorable, a physician`s presence is only necessary every second to third week. In our experience, TTCs can break, especially when used inappropriately or fitted to a heavy patient. Usually, the lifespan of a TCC in our experience is six to eight weeks. At each visit, the physician or wound care nurse who evaluates the patient should hold the TCC and try to squeeze the hindfoot area; when there is gross displacement a new TCC is required. Properly used, we have found that walkers rarely break.

It is important for both health care providers and patients understand that treating CO requires continuous pressure off-loading, even during the sleep and rest periods. Using a simple pillow is less effective for this purpose than commercially available heel protectors (Figure 2) [65]. Two studies have reported on the advantages of heel protectors in calcaneal ulcer healing [26, 66]. In these studies, in which patients were placed in an ankle-foot orthotic heel protector foam after undergoing partial calcanectomy (PC), or in an immobilizing boot with a plastic curved heel relief, primary healing was noted within one month in over 90% of patients [26, 66]. Once the CO has healed, off-loading should be continued as a secondary prevention, especially when severe neuropathy is present. For this purpose, custom-made orthopedic footwear works fine, as do insoles with a soft heel cup, or solid ankle-foot ortheses [8, 11, 12, 26, 58, 67, 68]. In case of ulceration regular professional wound care is essential. Available evidence suggests that local treatment with antiseptics or topical antibiotics, or hyperbaric oxygen therapy is generally not indicated [24].

Surgical management

The ultimate surgical goal in diabetic CO is to preserve limb and foot function as long as possible. CO can lead to bone fracture or expansion of infection to adjacent bone and articulations, with further destruction. The development of bacteremia or sepsis is uncommon, as the infection usually escapes through the calcaneal sinus tract. Infection can usually be eradicated by PC or total calcanectomy (TC), or if necessary a below-knee amputation (BKA) [8, 9, 11, 12, 58]. The average amount

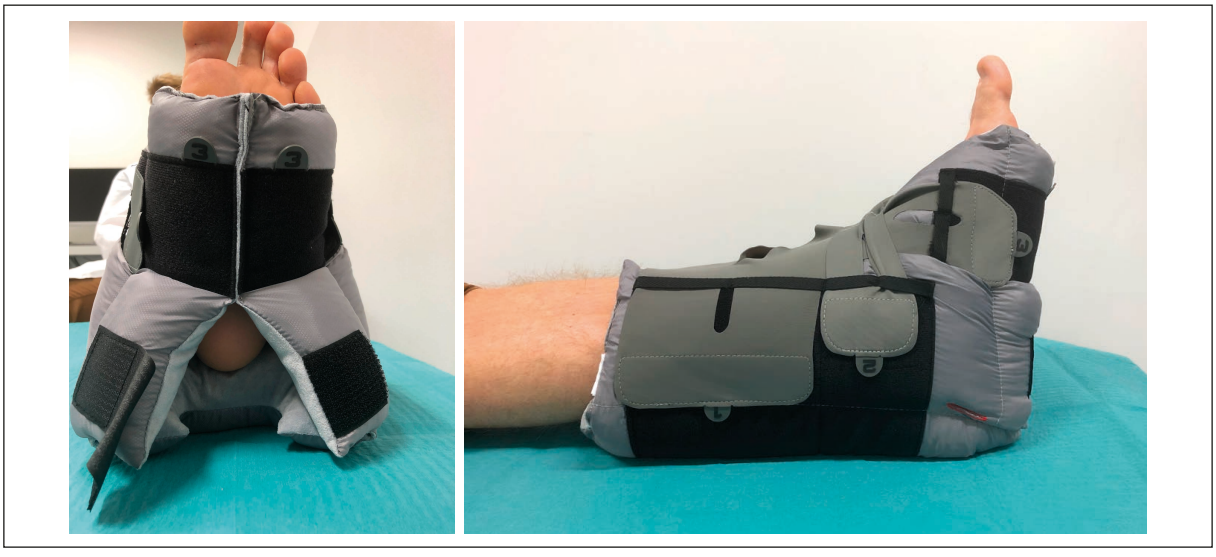

Figure 2 - Heel protector. Plantar view (closing straps left open to facilitate heel view) and lateral view.

of resected calcaneus by PC can vary between 13% and 74% [69]. When there is concomitant forefoot or midfoot osteomyelitis, Syme or Spitzy-Pirogoff amputations may be appropriate. While the former has the advantage of an end-weight-bearing stump, the latter is only a reasonable option when the CO occurs only in the *processus anterior calcanei* [70]. Both amputation techniques require that the patient has an open posterior tibial artery. When patency of the latter is not restorable, a transtibial amputation is indicated. In our experience, Syme amputations have two major problems. Firstly, the contact area is small and therefore, patients (especially with neuropathy) are prone to pressure ulcers. Secondly, the soft tissues need to be fixed to the distal tibia, otherwise medial (which we find occurs most often) or lateral soft tissue dislocation may occur. In order to achieve fixation, either the cartilage of the distal tibial has to be removed so that the cancellous bone and the soft tissues adhere, or the soft tissues must be fixated transosseously. Both techniques lead to exposure of previously uninfected bone, with the possibility of causing secondary osteomyelitis. A Spitzy-Pirogoff amputation includes a tibio-calcaneal arthrodesis, which would have to be performed by external fixation as internal fixation in case of osteomyelitis is inappropriate. The definitive decision on the type of surgery depends on the extent of the CO (as determined by the extent of loss of signal in MRI T1), the adequacy of arterial perfusion (especially regarding the posterior tibial artery), the amount of soft tissue loss, and the patient's preference [1, 9, 58, 67].

When there are no restrictions in the choice of surgical type, we recommend performing PC. This procedure allows the patient to be fitted with an orthopedic shoe when the surgical wound has healed, allowing nearly normal weight-bearing and the ability to walk without the severe compromise of energy expenditure that comes with a below knee amputation [71]. Patients undergoing TC usually need a prosthesis that is nearly the height of prosthesis required after below knee amputation. Further, an arthrodesis between the anterior border of the tibia, the talus and the midfoot may be necessary, as cranial dislocation of the foot often occurs after TC.

PC incurs the risk of tear-off fractures of the *tuber calcanei,* due to the tension of the Achilles tendon. In our experience, if more than 50% of the cranio-caudal diameter of the calcaneal tuberosity or most of the plantar cortical bone has to be resected, most patients will suffer from tear-off fractures. While the specific amount of cortical bone loss that leads to tear-off fractures has yet to be described, we usually perform Achilles tendon tenotomy in PC procedures. Further, we recommend Achilles tendon tenotomy if the tendon lies within the ulcer area. In this case, tenotomy will facilitate primary wound closure, which is generally the goal after PC or TC. There are no special suture techniques for calcaneal procedures that differ from those used for other areas of the foot. The most important consideration is ensuring a tension free wound closure, which, again, often requires doing an Achilles tendon tenotomy.

In the case of a PC with exposed cancellous bone, granulation tissue may be stimulated by use of a negative-pressure wound vacuum system, if primary wound closure is not possible. In case of TC, use of negative pressure therapy is also possible, but in our experience growth of granulation tissue usually takes longer as there is no cancellous bone exposed. The surgical wound should heal within three months; if not, suspect residual osteomyelitis or relapse of osteomyelitis.

We recommend performing transtibial amputation only in cases of concomitant mid- and forefoot ulcers that are refractory to established DFU treatment protocols, or in patients with Charcot arthropathy who have a rocker bottom or forefoot deformity that is prone to develop an ulcer. The presence of Charcot arthropathy itself is not always an indication for transtibial amputation in case of diabetic CO, as flattening of the medial foot arch leads to an elevated ground contact area of the foot and therefore facilitates local offloading of the heel.

Performing a PC or a TC is generally not demanding; it usually takes about 60-90 minutes and can be performed by one orthopedic surgeon assisted by a resident surgeon. The surgeons must bear in mind that these surgical procedures are meant to save the limb. The multitude of considerations that have to be made ultimately before choosing the type of surgery should lead to referral to an orthopedic surgeon who is experienced in the treatment of DFI and DFU as well as in performing transtibial amputations.

Lower extremity amputations are reconstructive surgeries that are technically demanding. Common mistakes in performing transtibial amputations are: cutting the fibula too long, thereby leading to lateral pressure ulcers; failing to round the distal anterior part of the tibia leading to anterior pressure ulcers; or, neglecting to shorten the sural, the peroneal or even the tibial nerves, leading to painful neuroma. This latter complication can prevent using a prosthetic device and therefore to an inability to walk. As tertiary care providers specializing in the field of diabetic foot complications, we frequently see patients suffering from one or more of the errors noted above.

We have summarized the literature on the frequency and performance of the three different resection surgeries described above in Table 4. As noted, a partial calcanectomy was performed in 81% (217/268), total calcanectomy in 8.6% (23/268) and below knee amputation (BKA) in 10% (28/268). However, these surgeries are no panacea. Limb loss (by subsequent BKA) after partial or total calcanectomy for CO is frequent, ranging in reported series from 0-67%, with an average failure rate of roughly 20% (Table 4). Crandall et al. revealed a secondary amputation risk of nearly 67% in diabetic CO cases, but all of the surgical procedures had been performed by orthopedic residents, rather than experience surgeons [9]. The retrospective review by Schade et al. on the outcomes of the three techniques (PC, TC, and BKA) found a fivefold greater amputation risk for diabetic CO compared to non-diabetic CO [10]. Minor revisions risks were 57% in PCs, 100% in TCs, and 28% in BKAs. Secondary amputations (mostly BKA) occurred in 29% of the PCs, in 50% of the TCs, and in 6% of the BKAs. Even TC as a surgical option did not diminish the failure risk [12].

When cutting bone, surgeons must not ignore properly caring for the soft tissues. Usually, we deal with soft tissue loss in one of three ways: 1) healing by secondary intention, with or without adding a negative-pressure vacuum-system; 2) developing a flap to cover the defect [4, 8, 58, 27, 72, 73]; or, 3) removing additional bone to manage

Table 4 - Outcome according to the surgical strategy from published articles with at least five cases of diabetic foot calcaneus osteomyelitis.

First author	*No, diabetic patients with calcaneal osteomyelitis*	*Initial type of surgery*			*Secondary amputation after PC / TC (%)*
		Partial calcanectomy (PC)	*Total calcanectomy (TC)*	*Below Knee Amputation*	
Crandall [9]	18	10	8	0	12 (66.7%)
Smith [67]	7	7	0	0	1 (14.3%)
Baumhauer [8]	6	6	0	0	1 (16.7%)
Laughlin [29]	21	7	0	8	0 (0%)
Baravarian [26]	12	12	0	0	0 (0%)
Chen [54]	11	11	0	0	0 (0%)
Goudie [66]	21	21	0	0	4 (19%)
Walsh [13]	7	0	7	0	2 (28.6%)
Shojaiefard [20]	18	18	0	0	0 (0%)
Faglia [14]	23	17	0	6	6 (35.3%)
Oliver [69]	35	35	0	0	12 (34.3%)
Drampalos [28]	12	12	0	0	0 (0%)
Dalla Paola [19]	18	18	0	0	0%
Akkurt [88]	23	23	0	0	1 (4.4%)
Waibel [12]	36	20	2	14	9 (40.9%)
Total	***268***	***227***	***23***	***28***	***48 (18%)***

tension free wound closure [29, 31]. As primary wound closure is preferable, removing additional bone is usually the first choice. When bone removal would compromise the residual contact area of the heel or enhance the risk of tear-off fractures, the second choice would usually be healing by secondary intention, usually with use of a VAC system. We consider using soft tissue flaps only in cases of severe soft-tissue loss. There seems to be no significant differences between pedicle muscle flaps and free flaps in the diabetic population [74].

An additional treatment the clinician should consider is passive physiotherapy to prevent equinus deformity, especially when Achilles tendon tenotomy has not been performed. Partial forefoot accentuated weight-bearing using an offloading device is permitted as soon as the wound has stopped oozing drainage. Once the surgical wound has healing, transition into orthopedic footwear, an adapted insole or a solid ankle-foot orthosis is indicated to prevent ulcer recurrence. Overall costs in the management of CO are often very high, but we failed to find specific data on this issue in the literature.

CONCLUSION

CO in the adult diabetic patient is a serious, potentially limb-treating condition that occurs in a small minority (7-8%) of DFI patients, mostly related to an overlying pressure ulcer. Other epidemiological differences of CO from DFI of other localizations are the rarity of associated bacteremia and the tendency to more often being associated with polymicrobial and Gram-negative infections in patients with long-standing diabetes mellitus. Therapeutically, the initial steps should be a combined multidisciplinary approach involving partial or total calcanectomy combined with targeted systemic antibiotic therapy of six weeks duration, eventually followed by secondary skin closures with flaps. Despite extensive therapeutic interventions, the risk of short-term therapeutic failure is about 20-30%. Adequate, individualized, and long-term pressure off-loading plays a crucial role in successful treatment. Clinicians cannot expect to see CO entirely resolve without them ensuring the reversal of the original underlying reason(s) leading to the infection. As even patients whose infection responds well in the short term may have late failure or recurrent infection, clinicians must provide and encourage the use of all possible preventive measures, including patient education, providing individually adapted footwear, and ensuring routine diabetic foot care [75, 90].

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REFERENCES

[1] Lipsky B.A., Aragón-Sánchez J., Diggle M., et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. *Diabetes Metab. Res. Rev.* 32, 45-74, 2016.
[2] Wang E.H., Simpson S., Bennet G.C. Osteomyelitis of the calcaneum. *J. Bone Joint Surg.* Br. 74, 906-909, 1992.
[3] Dalla Paola L., Carone A., Baglioni M., Boscarino G., Vasilache L. Extension and grading of osteomyelitis are not related to limb salvage in Charcot neuropathic osteoarthropathy: A cohort prospective study. *J. Diabetes Complications* 30, 608-12, 2016.
[4] Fukuda T., Reddy V., Ptaszek A.J. The infected calcaneus. *Foot Ankle Clin.* 15, 477-486, 2010.
[5] Levin L.S., Nunley J.A. The management of soft-tissue problems associated with calcaneal fractures. *Clin. Orthop. Relat. Res*. 290, 151-156, 1993.
[6] Taylor G.I., Palmer J.H. The vascular territories (angiosomes) of the body: experimental study and clinical applications. *Br. J. Plast. Surg.* 40, 113-141, 1987.
[7] . Comparison of bone preserving and radical surgical treatment in 32 cases of calcaneal osteomyelitis. *J. Bone Jt. Infect.* 1, 10-16, 2016.
[8] Baumhauer J.F., Fraga C.J., Gould J.S., Johnson J.E. Total calcanectomy for the treatment of chronic calcaneal osteomyelitis. *Foot Ankle Int.* 19, 849-855, 1998.
[9] Crandall R.C., Wagner F.W., Jr. Partial and total calcanectomy: a review of thirty-one consecutive cases over a ten-year period. *J. Bone. Joint. Surg. Am.* 63, 152-152, 1981.
[10] Schade V.L. Partial or total calcanectomy as an alternative to below-the-knee amputation for limb salvage: a systematic review. *J. Am. Podiatr. Med. Assoc.* 102, 396-405, 2012.
[11] Van Riet A., Harake R., Stuyck J. Partial calcanectomy: A procedure to cherish or to reject? *Foot Ankle Surg.* 18, 25-29, 2012.
[12] Waibel F.W.A., Klammer A., Gotschi T., Uçkay I., Boni T., Berli M.C. Outcome after surgical treatment of calcaneal osteomyelitis. *Foot Ankle Int.* 40, 562-567, 2019.
[13] Walsh T.P., Yates B.J. Calcanectomy: avoiding major amputation in the presence of calcaneal osteomyelitis-A case series. *Foot (Edinburgh, Scotland).* 23, 130-135, 2013.

[14] Faglia E., Clerici G., Caminiti M., Curci V., Somalvico F. Influence of osteomyelitis location in the foot of diabetic patients with transtibial amputation. *Foot Ankle Int.* 34, 222-227, 2013.
[15] Gariani K., Lebowitz D., von Dach E., Kressmann B., Lipsky B.A., Uçkay I. Remission in diabetic foot infections: Duration of antibiotic therapy and other possible associated factors. *Diabetes Obes. Metab.* 21, 244-251, 2019.
[16] Gidumal R., Evanski P. Calcaneal osteomyelitis following steroid injection: a case report. *Foot Ankle* 6, 44-46, 1985.
[17] Leigh W., Crawford H., Street M., Huang M., Manners S., Puna R. Pediatric calcaneal osteomyelitis. *J. Pediatric. Orthop.* 30, 888-892, 2010.
[18] Wronka K.S., Sinha A. Calcaneal osteomyelitis following steroid injection for plantar fasciitis: a case report. *Foot Ankle Spec.* 5, 253-255, 2012.
[19] Dalla Paola L., Carone A., Boscarino G., Scavone G., Vasilache L. Combination of open subtotal calcanectomy and stabilization with external fixation as limb salvage procedure in hindfoot-infected diabetic foot ulcers. *Int. J. Low Extrem. Wounds* 15, 332-337, 2016.
[20] Shojaiefard A., Khorgami Z., Mohajeri-Tehrani M.R., Larijani B. Large and deep diabetic heel ulcers need not lead to amputation. *Foot Ankle Int.* 34, 215-221, 2013.
[21] Gooding G.A., Stess R.M., Graf P.M., Moss K.M., Louie K.S., Grunfeld C. Sonography of the sole of the foot. Evidence for loss of foot pad thickness in diabetes and its relationship to ulceration of the foot. *Invest. Radiol.* 21, 45-48, 1986.
[22] Jan Y.K., Lung C.W., Cuaderes E., Rong D., Boyce K. Effect of viscoelastic properties of plantar soft tissues on plantar pressures at the first metatarsal head in diabetics with peripheral neuropathy. *Physiol. Meas.* 34, 53-66, 2013.
[23] Lung C.W., Hsiao-Wecksler E.T., Burns S., Lin F., Jan Y.K. Quantifying dynamic changes in plantar pressure gradient in diabetics with peripheral neuropathy. *Front. Bioeng. Biotechnol.* 4, 54, 2016.
[24] Lesens O., Desbiez F., Theis C., et al. *Staphylococcus aureus*-related diabetic osteomyelitis: medical or surgical management? A French and Spanish retrospective cohort. *Int. J. Low. Extrem. Wounds* 14, 284-290, 2015.
[25] Markakis K., Faris A.R., Sharaf H., Faris B., Rees S., Bowling F.L. Local antibiotic delivery systems: current and future applications for diabetic foot infections. *Int. J. Low. Extrem. Wounds* 17, 14-21, 2018.
[26] Baravarian B., Menendez M.M., Weinheimer D.J., Lowery C., Kosanovich R., Vidt L. Subtotal calcanectomy for the treatment of large heel ulceration and calcaneal osteomyelitis in the diabetic patient. *J. Foot Ankle Surg.* 38, 194-202, 1999.
[27] Chen S.L., Chen T.M., Chou T.D., Chang S.C., Wang H.J. Distally based sural fascio-musculocutaneous flap for chronic calcaneal osteomyelitis in diabetic patients. *Ann. Plast. Surg.* 54, 44-48, 2005.
[28] Drampalos E., Mohammad H.R., Kosmidis C., Balal M., Wong J., Pillai A. Single stage treatment of diabetic calcaneal osteomyelitis with an absorbable gentamicin-loaded calcium sulphate/hydroxyapatite biocomposite: The Silo technique. *Foot (Edinburgh, Scotland).* 34, 40-44, 2018.
[29] Laughlin R.T., Mader J.T., Calhoun J.H., Foad A. Calcaneal osteomyelitis: an analysis of aetiology and pathogenic organisms. *Foot Ankle Surg.* 5, 171-177, 1999.
[30] Mikami T., Kaida E., Yabuki Y., Kitamura S., Kokubo K., Maegawa J. Negative pressure wound therapy followed by basic fibroblast growth factor spray as a recovery technique in partial necrosis of distally based sural flap for calcaneal osteomyelitis. *J. Foot Ankle Surg.* 57, 816-820, 2018.
[31] Bibbo C., Stough J.D. Reduction calcaneoplasty and local muscle rotation flap as a salvage option for calcaneal osteomyelitis with soft tissue defect. *J. Foot Ankle Surg.* 5, 375-378, 2012.
[32] Jiang N., Ma Y.F., Jiang Y., et al. Clinical characteristics and treatment of extremity chronic osteomyelitis in Southern China: A retrospective analysis of 394 consecutive patients. *Medicine* 94, 1874, 2015.
[33] Frykberg R.G. Diabetic foot ulcers: pathogenesis and management. *Am. Fam. Physician.* 66, 1655-1662, 2002.
[34] Gariani K., Uçkay I., Lipsky B.A. Managing diabetic foot infections: a review of the new guidelines. *Acta. Chir. Belg.* 114, 7-16, 2014.
[35] Lipsky B.A., Peters E.J., Senneville E., et al. Expert opinion on the management of infections in the diabetic foot. *Diabetes. Metab. Res. Rev.* 28, 163-178, 2012.
[36] Math K.R., Berkowitz J.L., Paget S.A., Endo Y. Imaging of musculoskeletal infection. *Rheum. Dis. Clin. North. Am.* 42, 769-784, 2016.
[37] Dinh M.T., Abad C.L., Safdar N. Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. *Clin. Infect. Dis.* 47, 519-527, 2008.
[38] Newman L.G., Waller J., Palestro C.J., et al. Leukocyte scanning with 111In is superior to magnetic resonance imaging in diagnosis of clinically unsuspected osteomyelitis in diabetic foot ulcers. *Diabetes Care* 15, 1527-1530, 1992.
[39] Weinstein D., Wang A., Chambers R., Stewart C.A., Motz H.A. Evaluation of magnetic resonance imaging in the diagnosis of osteomyelitis in diabetic foot infections. *Foot Ankle* 14, 18-22, 1993.
[40] Yuh W.T., Corson J.D., Baraniewski H.M., et al. Osteomyelitis of the foot in diabetic patients: evaluation with plain film, 99mTc-MDP bone scintigraphy, and MR imaging. *AJR. Am. J. Roentgenol.* 152, 795-800, 1989.
[41] Desimpel J., Posadzy M., Vanhoenacker F. The many faces of osteomyelitis: A pictorial review. *J. Belg. Soc. Radiol.* 101, 24, 2017.

[42] Lee Y.J., Sadigh S., Mankad K., Kapse N., Rajeswaran G. *Quant. Imaging. Med. Surg.* 6, 184-198, 2016.
[43] Pineda C., Espinosa R., Pena A. Radiographic imaging in osteomyelitis: the role of plain radiography, computed tomography, ultrasonography, magnetic resonance imaging, and scintigraphy. *Semin. Plast. Surg.* 23, 80-89, 2009.
[44] Nicolaou S., Liang T., Murphy D.T., Korzan J.R., Ouellette H., Munk P. Dual-energy CT: a promising new technique for assessment of the musculoskeletal system. *AJR. Am. J. Roentgenol.* 199, 78-86, 2012.
[45] Pache G., Krauss B., Strohm P., et al. Dual-Energy CT virtual noncalcium technique: detecting posttraumatic bone marrow lesions-feasibility study. *Radiology* 256, 617-624, 2010.
[46] Jaramillo D. Infection: Musculoskeletal. *Pediatr. Radiol.* 41, 127-134, 2011.
[47] Gholamrezanezhad A., Basques K., Batouli A., Matcuk G., Alavi A., Jadvar H. Clinical nononcologic applications of PET/CT and PET/MRI in musculoskeletal, orthopedic, and rheumatologic imaging. *AJR. Am. J. Roentgenol.* 210, 245-263, 2018.
[48] Donovan A., Schweitzer M.E. Use of MR imaging in diagnosing diabetes-related pedal osteomyelitis. *Radiographics* 30, 723-736, 2010.
[49] Lauri C., Tamminga M., Glaudemans A., et al. Detection of osteomyelitis in the diabetic foot by imaging techniques: A systematic review and meta-analysis comparing MRI, White Blood Cell Scintigraphy, and FDG-PET. *Diabetes Care* 40, 1111-1120, 2017.
[50] Martin Noguerol T., Luna Alcala A., Beltran L.S., Gomez Cabrera M., Broncano Cabrero J., Vilanova J.C. Advanced MR imaging techniques for differentiation of neuropathic arthropathy and osteomyelitis in the diabetic foot. *Radiographics* 37, 1161-1180, 2017.
[51] Palestro C.J., Love C. Nuclear medicine and diabetic foot infections. *Semin. Nucl. Med.* 39, 52-65, 2019.
[52] Cohen M., Cerniglia B., Gorbachova T., Horrow J. Added value of MRI to X-ray in guiding the extent of surgical resection in diabetic forefoot osteomyelitis: A review of pathologically proven, surgically treated cases. *Skeletal. Radiol.* 48, 405-411, 2019.
[53] Cho S.H., Song H.R., Koo K.H., Jeong S.T., Park Y.J. Antibiotic-impregnated cement beads in the treatment of chronic osteomyelitis. *Bull. Hosp. Jt. Dis.* 56, 140-144, 1997.
[54] Chang W., Colangeli M., Colangeli S., Di Bella C., Gozzi E., Donati D. Adult osteomyelitis: debridement versus debridement plus Osteoset T pellets. *Acta Orthop. Belg.* 73, 238-243, 2007.
[55] Ferguson J.Y., Dudareva M., Riley N.D., Stubbs D., Atkins B.L., McNally M.A. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: a series of 195 cases. *Bone Joint J.* 96-B, 29-36, 2014.
[56] Gitelis S., Brebach G.T. The treatment of chronic osteomyelitis with a biodegradable antibiotic-impregnated implant. *J. Orthop. Surg. (Hong Kong)* 10, 53-60, 2002.
[57] Lazaro-Martinez J.L., Tardaguila-Garcia A., Garcia-Klepzig J.L. Diagnostic and therapeutic update on diabetic foot osteomyelitis. *Endocrinol. Diabetes Nutr.* 64, 100-108, 2017.
[58] Bollinger M., Thordarson D.B. Partial calcanectomy: an alternative to below knee amputation. *Foot Ankle Int.* 23, 927-932, 2002.
[59] Boulton A.J.M. The Diabetic Foot. In: Feingold K.R., Anawalt B., Boyce A., et al., eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2000.
[60] Bus S.A., van Deursen R.W., Armstrong D.G., Lewis J.E., Caravaggi C.F., Cavanagh P.R. Footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in patients with diabetes: a systematic review. *Diabetes Metab. Res. Rev.* 32, 99-118, 2016.
[61] Jeffcoate W.J., Lipsky B.A., Berendt A.R, et al. Unresolved issues in the management of ulcers of the foot in diabetes. *Diabet. Med.* 25, 1380-1389, 2008.
[62] Morona J.K., Buckley E.S., Jones S., Reddin E.A., Merlin T.L. Comparison of the clinical effectiveness of different off-loading devices for the treatment of neuropathic foot ulcers in patients with diabetes: a systematic review and meta-analysis. *Diabetes Metab. Res. Rev.* 29, 183-193, 2013.
[63] Petre M., Tokar P., Kostar D., Cavanagh P.R. Revisiting the total contact cast: maximizing off-loading by wound isolation. *Diabetes Care* 929-930, 2005.
[64] Lewis J., Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. The *Cochrane Database Syst. Rev.* 1, CD002302, 2013.
[65] Meyers T. Prevention of heel pressure injuries and plantar flexion contractures with use of a heel protector in high-risk Neurotrauma, Medical, and Surgical Intensive Care Units: A Randomized Controlled Trial. *J. Wound Ostomy. Continence Nurs.* 44, 429-433, 2017.
[66] Goudie E.B., Gendics C., Lantis J.C., 2nd. Multimodal therapy as an algorithm to limb salvage in diabetic patients with large heel ulcers. *Internat. Wound J.* 9, 132-138, 2012.
[67] Smith D.G., Stuck R.M., Ketner L., Sage R.M., Pinzur M.S. Partial calcanectomy for the treatment of large ulcerations of the heel and calcaneal osteomyelitis. An amputation of the back of the foot. *J. Bone Joint Surg. Am.* 74, 571-576, 1992.
[68] Fuchs M., Burchhardt H., Dresing K., Radebold T., Stürmer K.M. Resection of the calcaneus as a treatment option in osteitis following an open calcaneus fracture. *Unfallchirurg* 103, 602-606, 2000.
[69] Oliver N.G., Steinberg J.S., Powers K., Evans K.K., Kim P.J., Attinger C.E. Lower extremity function following partial calcanectomy in high-risk limb salvage patients. *J. Diabetes Res.* 2015, 432164, 2015.
[70] Hornby R., Harris R. Syme's amputation. Fol-

low-up study of weight-bearing in sixty-eight patients. *J. Bone Joint Surg. Am.* 57, 346-349, 1975.
[71] Pinzur M.S., Gold J., Schwartz D., Gross N. Energy demands for walking in dysvascular amputees as related to the level of amputation. *Orthopedics* 19921033-19921036, 1992.
[72] Jin H.B, Kim K.S. Versatility of the reverse sural fascio-cutaneous flap for the reconstruction of lower leg defects caused by chronic osteomyelitis. *Arch. Plast. Surg*. 45, 601-604, 2018.
[73] Ignatiadis I.A., Tsiampa V.A., Galanakos S.P., et al. The reverse sural fasciocutaneous flap for the treatment of traumatic, infectious or diabetic foot and ankle wounds: A retrospective review of 16 patients. *Diabet. Foot Ankle* 2, 2012.
[74] Ducic I., Attinger C.E. Foot and ankle reconstruction: pedicled muscle flaps versus free flaps and the role of diabetes. *Plast. Reconstr. Surg.* 128, 173-180, 2011.
[75] Bus S.A., Armstrong D.G., van Deursen R.W., et al. IWGDF guidance on footwear and offloading interventions to prevent and heal foot ulcers in patients with diabetes. *Diabetes Metab. Res. Rev.* 32, 25-36, 2016.
[76] Flieger S. Langfristige Ergebnisse der operativen Therapie bei Kindern mit Osteomyelitis. Doctoral thesis. *Medizinische. Fakultät. der. Westfälischen. Wilhelms-Universität. Münster.* 1-102, 2006.
[77] Kurvin L. Rekonstruktive Chirurgie bei infizierter neuropathischer Osteoarthropathie des Rückfußes. Doctoral thesis, *Medizinische. Fakultät. Der. Universität. München*. 2009.
[78] Ghods M., Grabs R., Kersten C., Chatzopoulos P.P., Geomelas M. A modified free muscle transfer technique to effectively treat chronic and persistent calcaneal osteomyelitis. *Ann. Plast. Surg.* 68, 599-605, 2012.
[79] Boffeli T.J., Collier R.C. Near total calcanectomy with rotational flap closure of large decubitus heel ulcerations complicated by calcaneal osteomyelitis. *J. Foot Ankle Surg*. 52, 107-112, 2013.
[80] Schachinger I. Klinische und epidemiologische Aspekte der Osteomyelitis im Kindes- und Jugendalter. Doctoral thesis. *Medizinische. Fakultät. der. Universität Graz., Austria.* 2014.
[81] Aragon-Sanchez J., Lazaro-Martinez J.L., Alvaro-Afonso F.J., Molines-Barroso R. Conservative Surgery of diabetic forefoot osteomyelitis: how can i operate on this patient without amputation? *Int. J. Low Extrem. Wounds* 14, 108-131, 2015.
[82] Iwakura T., Lee S.Y., Niikura T., et al. Gentamycin-impregnated calcium phosphate cement for calcaneal osteomyelitis: a case report. *J. Orthoped. Surg. (Hong Kong).* 22, 437-439, 2014.
[83] Babamahmoodi F., Shokohi T., Ahangarkani F., et al. Rare Case of *Aspergillus ochraceus* osteomyelitis of calcaneus bone in a patient with diabetic foot ulcers. *Case. Rep. Med.* 2015, 509827, 2015.
[84] Grecian S.M., Haycocks S.J., Chadwick P.R., Young R.J., Paisley A.N. Characteristics of calcaneal osteomyelitis: an unusual and severe form of diabetic foot disease. *Br. J. Diabetes Vasc. Dis.* 15, 166-168, 2015.
[85] Memiş A., Mutluoğlu M., Öztürk S., Kara K., Ay H. Calcaneal osteomyelitis associated with a severe abscess. *J. Am. Coll. Clin. Wound Spec.* 6, 53-56, 2014.
[86] Evran M., Sert M., Tetiker T., Akkuş G., Biçer O.S. Spontaneous calcaneal fracture in patients with diabetic foot ulcer: Four cases report and review of literature. *World. J. Clin. Cases* 4, 181-6, 2016.
[87] Allen L.L., Kalmar G., Driver V.R. Treatment of a high-risk diabetic patient with peripheral vascular disease and osteomyelitis. *Tech. Vasc. Interv. Radiol*. 19, 96-100, 2016.
[88] Akkurt M.O., Demirkale I., Öznur A. Partial calcanectomy and Ilizarov external fixation may reduce amputation need in severe diabetic calcaneal ulcers. *Diabet. Foot Ankle* 8, 1264699, 2017.
[89] Lin C.T., Chen C.Y., Chen S.G., Chen T.M., Chang S.C. Preserve the lower limb in a patient with calcaneal osteomyelitis and severe occlusive peripheral vascular disease by partial calcanectomy. *J. Med. Science.* 35, 74-78, 2015.
[90] Uçkay I., Jornayvaz F.R., Lebowitz D., Gastaldi G., Gariani K., Lipsky B.A. An overview on diabetic foot infections, including issues related to associated pain, hyperglycemia and limb ischemia. *Curr. Pharm. Des.* 24, 1243-1254, 2018.