Ankle Infections: Postoperative and Septic Arthritis

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1 Introduction and Epidemiology

Ankle infections encompass a broad spectrum of pathology which can lead to significant morbidity. Careful preparation and adherence to treatment principles, along with a thorough understanding of the epidemiology and risk factors, as well as the diagnostic and treatment options can lead to a successful outcome.

Here, we will focus on native ankle septic arthritis and postoperative ankle infections with particular emphasis on fracture related infections (FRI) and those involving hardware. Postoperative infections can arise in the elective setting or post-traumatic with injuries being categorized as high and low energy, and open versus closed with somewhat different implications. It is helpful to identify the depth of infection as being confined to the skin structures as a cellulitis, or deeper more aggressive infections forming abscesses and necrosis, and those involving the joint space or bone such as osteomyelitis. Additionally, it is useful to stratify infections by duration as either acute (typically less than 4–6 weeks) or chronic.

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Soft tissue infections can occur more readily in the ankle due to impaired perfusion and altered sensation that may be preexisting in the patient [1]. One epidemiological study found an incidence of cellulitis of 199 cases in 100,000 person-years, with a 21.6% rate of hospitalization and recurrence [2]. Postsurgical patients most often present acutely with cellulitis. These patients are at a high risk due to preexisting skin insult and lymphatic drainage interruption [1]. While cellulitis is typically treated with antibiotics alone, the presence of deep space infections may require operative intervention [3]. Therefore, determination of the depth of infection and any abscess formation is key and relies both on careful examination and, frequently, advanced imaging.

The incidence of septic arthritis has been reported to be from 2 to 10 cases per 100,000 persons, with approximately 3–7% of the cases involving the foot or ankle [4]. Postoperative ankle joint infections have been reported in 1–5% of cases most commonly through direct inoculation with typical skin flora [3]. Therefore, the best treatment of postoperative infections, is prevention.

Osteomyelitis represents a deep infection that has invaded the bony architecture. An important distinction must be made between an acute osteomyelitis, representing vascularized viable bone, and chronic osteomyelitis with bone necrosis. Whereas the former may often be treated with systemic antibiotics, the later always requires a debridement for eradication.

D. Herscovici Jr. et al. (eds.), *Evaluation and Surgical Management of the Ankle*,
https://doi.org/10.1007/978-3-031-33537-2_19

2 Risk Factors for Infection

A thorough understanding of the risk factors associated with ankle infection will help tailor the clinician's index of suspicion for diagnosis and prognostication. Recognizing those factors that are modifiable can aid in treatment.

Injury related risk factors are nonmodifiable. Traumatic ankle injuries are at baseline elevated risk for infection compared to elective surgery. Tissue disruption and devascularization from the injury impede the body's native defenses [3]. Specifically, open fractures, high-energy mechanisms, and wound contamination level each confer a statistically significant increased risk of developing a surgical site infection [5]. Higher energy injuries such as tibia plafond fractures have historically had an elevated risk of wound breakdown and infection with historic rates of infection after acute operative treatment from 13 to 50% [6–8]. While the injury itself is not modifiable, the use of a staged treatment protocol with spanning external fixation (Fig. 1), elevation for edema resolution and delayed internal fixation can reduce the rates of wound breakdown and deep infection to about 5% [6].

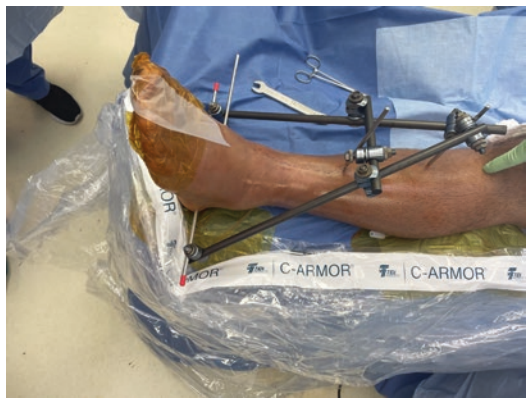

Fig. 1 Shows a patient with a high energy pilon fracture who underwent temporary ankle spanning external fixation in the acute phase to allow for improvement in the swelling and the damaged soft tissue envelope. Careful inspection now reveals transverse extensor surface skin creases at the ankle joint, and the longitudinal stress-relaxation stretch marks in the skin indicative of resolution of the swelling phase

Patient-related risk factors which compromise immune surveillance, metabolism, and vascularity are critical to identify. It is helpful to think of patient risk factors as systemic and local factors. Systemic factors include malnutrition, renal failure, liver failure, diabetes, chronic heart disease, alcohol use, tobacco use, steroids, immunodeficiency, malignancy, obesity, and extreme age [9, 10]. Local factors include lymphedema, venous stasis, peripheral vascular disease, and localized scarring and fibrosis [9]. Patients with any of these factors have been termed a compromised host or "Class B" host, and nearly 80% of osteomyelitis cases are reported in class B hosts [9].

While not all patient factors are modifiable, those which are should be addressed preoperatively in elective surgery cases. Nutritional status should be optimized, with the involvement of a nutritionist in a multidisciplinary team. Patients should be counseled on smoking cessation and reduction of excessive alcohol consumption. Smoking has been identified as an independent risk factor in the failure of treatment in fracture related infections [11]. American Society of Anesthesiologists (ASA) grade $\geq$3 has been found as an independent risk factor for infection, thus for elective procedures patients should be medically optimized by their primary physician [5]. Obesity has been routinely found as an infection risk factor with Body Mass Index (BMI) $\geq$30 carrying a significant increased risk [5, 12]. However, in the acute traumatic setting, modification of these factors is usually not an option. Additionally, for patients with degenerative pain in the lower extremities, often exercise and weight reduction is painful leading to a vicious cycle begetting further comorbidities such as diabetes and heart disease further elevating their risk [13].

Diabetes mellitus is worth a special note ankle infection. The overall risk of any foot and ankle infection in diabetic patients is eight times higher than that of the general population and postoperative infection rates double that of healthy cohorts [14]. Additionally, diabetics have a blunted immune response to infection leading to lower cure rates and as a result a significantly higher risk of amputation after infection [15]. One report

found a postoperative infection rate up to 60% and amputation rates up to 42% in diabetic open ankle fractures [16]. There is a clear association between glucose control and postoperative surgical site infections, with Jupiter et al. demonstrating a significant risk of infection development with hemoglobin A1c greater than 7.0% [17]. Hyperglycemia, even without a diagnosis of diabetes, has been identified as an independent risk factor for infection in orthopaedic trauma patients. Blood glucose levels ≥200 mg/dL on presentation is a significant risk factor in the development of both 30 and 90 day deep surgical site infection [18, 19]. In situations where surgical delay for improved diabetic management is not feasible, tight perioperative glucose control is a requirement and close follow up with a multidisciplinary team post-op can improve the chances of a good outcome. Finally, special attention must be paid to diabetic patients with ulcers not only for local reasons but also due to the risk of seeding infection at an ankle surgical site. All factors must be addressed when treating diabetic ulcers, including nutritional status and shoe wear modifications.

Age over 65 has been associated with higher infection rates and can be attributed to their higher risk of associated medical comorbidities, such as declining nutritional state, declining mental capabilities, and decreased mobility [13]. One study found that age was an independent risk factor for infection that linearly increased up to age 65, but thereafter paradoxically decreased. The authors proposed the "hardy survivor" effect, as a possible explanation [20]. While many of the factors associated with age are nonmodifiable, these serve to guide index of suspicion as well as prognostication.

2.1 Surgeon and Surgery-Related Risk Factors

Many risk factors for infection are directly under the surgeon's control. These factors include issues such as surgical time, soft tissue handling, antibiotic usage, and post-operative protocols. The Surgical Care Improvement Project (SCIP) guidelines lay out several controlled variables [21]. (1) Prophylactic antibiotics should be received within 1 h prior to incision [21]. Infection rates are significantly higher in cases that are not given preoperative antibiotics compared to those that are [22]. Additionally, for longer procedures, the antibiotics should be redosed after two half-lives (about every 4 h for cefazolin) [23]. (2) Prophylactic antibiotics should be selected for activity against the most probable microbe, in this case *Staphylococcus aureus*. (3) Euglycemia should be maintained, with well-controlled morning blood glucose concentrations on the first two postoperative days. (4) Hair at surgical site should be removed with clippers, not with a blade. (5) Urinary catheters should be discontinued within 2 postoperative days. (6) Normothermia should be maintained perioperatively [21]. Appropriate surgical site preparation can improve infection risks and postoperative outcomes. The foot may contain up to three million microorganisms/cm^2 [13]. Using an alcohol-based skin prep prior to surgical incision is a mandatory step. Studies have shown that chlorohexidine is superior in decreasing bacterial load [24].

Regarding operative time, any increase in time between surgical incision and finished closure allows for more contamination of the surgical wound, increasing the risk for surgical infection [13]. While we are not aware of any set surgical time limit above which infection rates dramatically increase, cases in excess of 90 min of open wound time have a higher odds ratio of infection [5]. The surgeon should aim to be both expedient and thorough. Careful preoperative planning with contingencies will minimize tinkering time in the OR, and a surgical plan will avoid against missed steps keeping the case moving.

The most directly controllable factor is surgical technique and soft tissue handling. Overly aggressive stripping and retraction causes disruption of the microvasculature, leading to ongoing ischemia and impeded local host infection defense. Open fractures and fracture related infections (FRIs) require careful debridement of all necrotic tissue including skin, muscle, fascia, and bone when needed. Focusing on a small

exposure may lead to incomplete debridement and persistent nonviable and infected tissue. Additionally, good hemostatic technique should be observed to avoid postoperative hematoma and dead space for bacteria to thrive.

3 Diagnosis

Evaluation of a patient with suspected ankle infection begins with a detailed history and physical examination. Special attention should be given to patient comorbidities and risk factors for infection [25]. History should include any prior injury or surgery, evaluation of onset and duration of symptoms, fever and chills (not always present), malaise, pain, weightbearing tolerance, history of prior infections anywhere, and general medical health [1]. Often patients with ankle infections will exhibit no systemic signs of infection such as fever (only seen in 30–40% cases) [25, 26].

Physical exam should pay attention to the cardinal signs of infection (swelling, redness, tenderness, and warmth), surgical scars, draining sinus, lymphedema, skin health including induration and assessment of vascular status (shiny skin, alopecia, venous insufficiency). Attention should be given to localization of the infection, the most important aspect being the depth of infection. While cellulitis will be tender to touch, marked tenderness along the joint line and extreme pain with minimal joint motion of the ankle may be indicative of a septic arthritis [25].

Necrotizing fasciitis is beyond the scope of this chapter but deserves a brief note. It represents a rare but very aggressive deep necrosing infection, occurring usually in immunosuppressed patients, spreading rapidly along the myofascial planes. The hallmark clinical history and exam are extreme pain out of proportion to exam, often appearing early like a cellulitis with erythema, warmth, tenderness, and tachycardia. Delay in diagnosis contributes to the high reported mortality rate of 50–70% from septic shock [1, 3, 27, 28]. Blisters and bullae can develop but these are usually intermediate to late findings. One of the most consistent findings is progression of erythema and symptoms despite an adequate intravenous antibiotic regimen, highlighting the importance of serial exams, and a high index of suspicion for diagnosis. Classically these patients can deteriorate rapidly with hallmark depletion of their serum sodium and declining renal function. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score can aid in diagnosis but should not replace clinical judgement. The treatment for necrotizing fasciitis involves an emergent widely based debridement of all necrotic skin, subcutaneous tissue and fascia, and broad spectrum IV antibiotics [1, 3, 27, 28].

3.1 Labs

Peripheral blood tests in the workup of a suspected ankle infection of any kind include peripheral blood cultures (typically two sets), complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels. However, these markers only represent inflammation in the body and thus have a poor specificity [25]. In a review of 30 patients with native septic ankles, Holtom et al. reported elevated ESR and CRP in all patients, but only 47% had elevated peripheral WBC [29]. We find it useful to also check a HgA1c in patients, as uncontrolled diabetes is a strong risk factor for infection, but also, we have not infrequently uncovered a new diagnosis of prediabetes or diabetes in a patient. If the suspected infection is postoperative and there are wound healing issues, we recommend also checking metabolic and nutrition labs such as basic metabolic panel (chem-7), thyroid panel, prealbumin, and albumin levels [10]. Total lymphocyte count of <1500 cells/mm^3 and albumin <3.5 mg/dL, and serum transferrin <200 mg/dL are indicative of malnutrition and reduced ability to heal a wound [30]. It is useful to consult a nutrition expert in the case of these patients.

3.2 Aspiration and Tissue Culture

If infection involving the joint is suspected then the gold standard in diagnosis is an aspiration of synovial fluid [25]. This is typically done with an

18G hypodermic needle attempting to avoid apparent cellulitic skin. This may be done either anteromedial, just medial to the palpable tibialis anterior tendon at the level of the joint line aiming into the superomedial joint gutter, or alternatively through an anterolateral approach midway between the anterior border of the fibula and the peroneus tertius at the level of the joint [25]. Traditionally a synovial WBC count >50,000 cells/mm^3 has been used for a diagnostic threshold of septic native arthritis around the body [25, 31]. Data should be interpreted with caution and respect to the pretest clinical suspicion as a cutoff of 50,000 has been shown to have sensitivity of only 64% [31]. Fluid should be sent for culture, gram stain, and crystal analysis. Culture remains the gold standard for diagnosing a septic joint, however up to 20% of patients with septic ankles have been reported to be culture negative [29].

Regarding draining wounds, cultures should be obtained from deep tissue in the operating room (discussed in section below). We do not recommend superficial tissue or fluid samples nor routine culture swabs as these have a low diagnostic yield [32–35].

3.3 Imaging

Imaging can be a substantial aid to appropriate diagnosis and treatment plans. Plain radiographs should routinely be obtained in evaluation. In postoperative settings, radiographs should be scrutinized for maintenance of reduction and alignment, change in implant position or any lucent halo which may indicate loosening. Early in an infection, radiographs may only show soft tissue swelling, but with delayed presentations of septic arthritis there may be evidence of joint destruction. Late changes in bony structure can also be evaluated on plain radiographs, including cortical erosion and periosteal reactions. It is mandatory to examine radiographs for the presence of subcutaneous gas, which in the absence of an open wound, raises concern for an aggressive necrotizing infection [25].

Computed tomography (CT) is more sensitive to bony and joint destructive changes, and if renal function allows, the addition of contrast is very useful in looking for deep soft tissue abscess in postoperative infections [25]. This is instrumental in debridement planning as when extensile measures are needed for identifying skip abscesses. In fracture cases, CT is useful in assessing union. This is important if a question exists about the necessity for hardware retention.

In subacute postop infections, we have found MRI to be useful in looking for bony edema tracking up the marrow space away from the local hardware which might be indicative of intramedullary osteomyelitis which may necessitate reaming of the marrow space. The addition of contrast to MRI enhances evaluation for soft tissue abscess [25, 36]. For native septic arthritis, we do not recommend routine CT or MRI scanning unless something atypical in the history or physical leads to suspicion of soft tissue abscess or bony extension. Tagged WBC bone marrow scintigraphy with technetium-99 m sulfur colloid has been reported with 86–98% accuracy in prosthetic joint infections [25], however we have not found this to be particularly useful in the non-arthroplasty setting.

Vascular studies, such as palpation or doppler of the distal pulses, can provide valuable information about the potential to heal any wounds or infections. Knowledge of any insufficiency is critical in surgical planning of a debridement in assessing whether primary or secondary healing is viable or whether flap coverage will be required. Ankle-Brachial Index (ABI) >0.9 is considered normal, with a value <0.45 concerning for a poor healing response. A toe wave pressure of 0.45 is predictive of good healing while a pressure of 0.2 is indicative of poor healing. Duplex ultrasonography can assess for arterial stenosis and occlusive venous insufficiency, which may warrant referral to vascular surgery for consideration of intervention angiography [1].

4 Treatment

Once a diagnosis of infection has been established the management depends upon the presence or absence of joint involvement, amount of

joint degeneration, presence or absence of fracture, instability, presence of hardware, and extent of bony involvement.

Treatment requires an aggressive surgical debridement of all infected and all nonviable tissues. Compromised tissue left in place provides a nidus for persistent infection and bacterial adherence with biofilm formation [33]. Several biopsies of both soft tissue and bone should be taken at the time of the initial debridement as routine swab cultures and aspiration have been shown to not be representative of the chronic infection and adherent bacteria [33].

A brief word about urgency and antibiotics. Lee et al. reported that patients who were treated with antibiotics with or without debridement or aspiration within 5 days of symptom onset had a greater chance to regain ankle function, although most ankles still had residual mild or severe pain at the time of the latest follow-up [37]. Treatment of infections is urgent but should be stepwise with a prioritized goal of a targeted diagnosis. We do not recommend an initial treatment course of antibiotics be started until a deep culture can be obtained, unless based on clinical evaluation you have determined the infection to be superficial cellulitis only. The only other exception to this rule is in the physiologically septic patient, who should be promptly started on empiric broad spectrum antibiotics immediately after obtaining blood cultures [25].

4.1 Native Septic Joint Arthroscopic or Aspiration

The mainstay of management of ankle joint infections is an operative debridement. Serial aspirations have been reported with success in the treatment of native septic ankles [25]. However, this excludes cases with hardware or extra-articular involvement, and it is the author's opinion that aspiration should be reserved for the medically infirm and end-stage arthritic joints.

Arthroscopic debridement has been used in ankle infections and reported favorable outcomes with smaller incisions, shorter hospitalization, and more rapid rehab compared with open arthrotomy [25, 38]. Typical portals are anteromedial and anterolateral (similar to aspiration sites) with one for an inflow with a 4 mm 30° scope and the other as an outflow or working portal for an arthroscopic shaver [25]. An arthroscopic debridement does not allow for addressing extra-articular extension or hardware in FRIs and should be relegated to native septic arthritis.

4.2 Fracture Related/Hardware

Fracture related infections are distinct from native septic arthritis or osteomyelitis as well as from infected periprosthetic joints in the matter of instability. Stability of the tissue not only lessens ongoing damage to surrounding tissue, but also creates an environment favorable to infection resistance [39–41]. However it is well known that metal implants involved in an infection allow for bacteria to form a biofilm, consisting of a glycocalyx which confers significant resistance to both the body's immune response as well as to antibiotics [33, 39, 42].

Thus, in the care of fracture related infections there are two objectives which somewhat oppose one another which are the eradication of infection, impeded by the presence of a foreign body, and the need for stability both for fracture union and a favorable environment for infection clearance.

More specifically, the primary aims of treatment of fracture related infections can be stated as:

1. Fracture consolidation.
2. Eradication of infection at final treatment.
3. Healed soft tissue envelope.
4. Restoration of function.
5. Prevention of chronic osteomyelitis [43].

Rittman and Perren stated that the stabilizing effect of implants outweighed the disadvantage of the foreign body effect [41]. It has thus been recommended that hardware should be retained in the face of infection until fracture healing so long as the hardware is stable and functioning [44]. Therefore, two concepts have been laid out

in consideration. Firstly, debridement, antimicrobial therapy, and implant retention, so called "DAIR" protocol. Secondly, debridement, antimicrobial therapy, and implant removal or exchange. The determination of what to do with the hardware is influenced by the time from injury, extent of bony healing and stability, amount of necrotic tissue and dead space, maintenance of acceptable fracture alignment, and implant fixation and contribution to stability [43, 45].

One proposed treatment algorithm is to attempt to maintain hardware in a patient presenting up to 10 weeks out from the time of surgical fixation. Although 10 weeks is a rather arbitrary number, it should serve as a treatment guide depending upon the abovementioned factors. These patients should undergo a debridement and retention of hardware, if stable and still functional, or removal of hardware if it is loose. This is not intended as a definitive treatment, but rather as a temporizing measure to suppress the infection long enough to allow for fracture healing and stability so that the hardware could be removed later. In patients presenting greater than 10 weeks from ORIF, the fracture is presumed to have enough stability and they undergo a debridement and removal of hardware [16].

The final consideration in what to do with hardware regards the alignment of the fracture. In those patients who have lost acceptable alignment and the fracture is not united, we will either remove the hardware, perform a debridement and then revision reduction, and internal fixation. Or if there is purulence at the time of debridement we will remove the implants, perform a debridement, use local antibiotics (described later), and plan for revision fixation later after wound sterilization. In such cases a spanning external fixator is applied to provide bony and soft tissue stability, as an antibiotic intramedullary rod will not function well so distally; rarely a splint may suffice.

When hardware must be retained for the stability of the fracture and to aid in initial treatment of infection, the decision must be made as to whether those implants should be taken out later. In a review of 69 infected fractures managed with hardware in place, Rightmire et al. reported a disappointing 68% union rate, with the remaining requiring hardware removal or exchange ultimately. Furthermore, they reported in those with successful union, the rate of infection recurrence in those with hardware left in place was 32% compared to 16% in those who had hardware removed after union. They recommend strong consideration of hardware removal and debridement after obtaining fracture union [11].

In the case of chronic osteomyelitis, treatment is determined by four factors; the condition of the host, the functional impairment caused by infection, the site of involvement, and the extent of bony necrosis [9]. Concomitant adjacent osteomyelitis has been reported in 30% of patients with septic arthritis, and is most commonly found in compromized hosts with one or more risk factors. In such patients, the clinician should have an elevated index of suspicion, and it may be useful to obtain an MRI of the foot and ankle to evaluate for adjacent osteomyelitis [29].

4.3 Tissue Sampling

Deep tissue samples are recommended to be sent for both microbiological as well as histopathological examination. Multiple samples should be taken, each with a new clean surgical instrument and each in a separate tissue culture bottle for aerobic and anaerobic growth [32, 43, 46]. These should preferentially be taken from suspected areas of fracture related infection, such as periosteum and membrane at implant bone interface and care to avoid the skin and any superficially draining areas. We recommend multiple, at least three to five, deep samples be taken from distinct areas of the wound. Multiple samples growing the same organism avoid confusion over a single sample possibly growing a known skin contaminant. Regardless of number of samples, it is important to be systematic and even develop a protocol in the approach to biopsies as this has been found to have a higher diagnostic yield than random sampling and no protocol for antibiotic management [32]. We do not recommend superficial tissue or fluid samples nor routine culture

swabs as these have a low diagnostic yield [32–35]. We do not recommend any additional biopsies or cultures be taken at final debridement as we have not found this to be helpful in changing management. The most accurate biological diagnosis would be the one from the initial biopsy and cultures, and treatment should be based on those.

Novel techniques for diagnostics include genomic sequence identification such as Next-generation sequencing through 16s rRNA gene profiling have been reported to identify organisms in 77% more cases than traditional microbiological identification techniques in fracture nonunion biopsies. These genetic material profiling techniques may provide a way to identify further infections in cases which otherwise would be classified as "culture negative" infections. We have not yet instituted this in our practice, but promising results are coming out of the arthroplasty literature [47].

4.4 Debridement

Irrigation and debridement remain the keystone in the treatment of fracture related infections. Surgical approach will typically proceed through prior surgical incisions, and strict careful soft tissue handling techniques are critical to maintain a viable soft tissue envelope [48]. The purpose of irrigation is reduction of bacterial load and the removal of loose debris. The optimum volume of fluid is unknown but should be sufficient to macroscopically clean the entire wound bed [49].

Debridement should be systematic and thorough with the goal of removing all necrotic bone, necrotic and ischemic soft tissue, and any nonessential or nonfunctioning foreign bodies (e.g., braided suture and loose hardware). When using prior incisions, any local sinus tracts should be excised. It may be beneficial to excise a few millimeters of dense adherent scar tissue not contributing to healing on either side of the incision. Preoperative planning should include a strategy for management of any soft tissue defects if primary closure will be complicated by an adequate debridement. Often inflamed tissue will retract significantly after debridement, amplifying the apparent tissue loss in the limited realestate about the ankle (Fig. 2). Accessory sinus tracts remote from intended debridement approach may be left as these will typically close secondarily after the infection is treated [48].

If it is determined that further bone exposure beyond the initial surgical bed is needed, this should proceed in an extraperiosteal plane to preserve vascularity to the bone [48]. The extent of debridement of bone requires careful inspection and clinical judgement and will be affected by duration of infection. In general, all bone left behind should have bleeding surfaces, following the theory that bleeding infected bone may heal with systemic antibiotic therapy [43]. Bilgili et al. showed that in the face of infection with hardware, fracture healing proceeds in a histopathologically similar albeit slower manner to uninfected tissue. In a rat model fracture callus was shown to have lower stiffness and torque to failure at 6 weeks compared with uninfected tis-

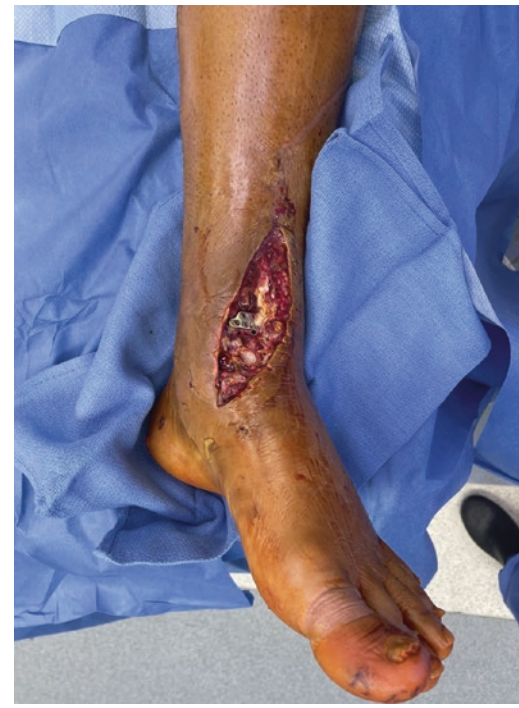

Fig. 2 Shows significant retraction of tissue exacerbating the apparent tissue loss after a debridement of an infected pilon fracture

sue [50]. In chronic infections (>6 to 10 weeks duration), bony debridement should proceed until uniform petechial bleeding bone surfaces are encountered (the so called "paprika sign") [9, 48].

The number of debridements required in fracture related infections has been reported from 1 to 11 with an average number of 3 debridements [11]. In chronic osteomyelitis cases, the average number of debridements has been reported as 3.8 [9]. In FRI requiring hardware retention, if purulence is found on initial debridement, we recommend serial irrigation and debridement until no further purulence is encountered before definitive closure or coverage.

In native septic ankles or in FRI diagnosed early and with no obvious purulence and having viable soft tissue envelope amenable to primary closure, a single irrigation and debridement may be sufficient. In these, careful serial exams and laboratory trend may show improvement on systemic antibiotics. In these we have followed a protocol developed by the senior author for incision management and monitoring. Wounds which are closed have a closed incisional vacuum (ciVAC) dressing applied for 72 h and are then changed to a dry gauze dressing for 12 h to evaluate for persistent drainage. Wounds with drainage, other than wound edge oozing, should have a new ciVAC dressing applied for another 72 h and the protocol is repeated. This is followed for three sequential ciVACs cycles, or about 9–10 days after which if the wound drainage has not noticeably decreased a repeat irrigation and debridement is performed and the protocol is restarted.

We apply these ciVACs with an open cell polyurethane ether sterile foam dressing applied to a broad surface area encompassing the incision and surrounding inflamed skin. We use a layer of nonadherent emollient gauze under the foam sponge to prevent skin irritation. This not only aids in drainage management and monitoring, but also provides a durable sterile dressing for the wound, promotes blood flow to the local area, and reduces edema through the incision. The rationale behind a broad surface is to apply even pressure to decrease shear forces in the wound bed. However, others have advocated for a strip of polyurethane ether sponge applied directly to the skin in a narrow strip encompassing just the incisional margins, while still others have advocated for use of a polyvinyl alcohol white sponge to decrease skin irritation [51, 52]. We prefer to use −125 mmHg pressure at a low continuous setting. Others have reported use on closed incisions ranging from −50 to −200 mmHg [52, 53].

4.5 Local Antimicrobial Therapy

Local administration of antimicrobials is an effective means of managing 'dead space' and allows for administration of a supra-therapeutic dose of antibiotics not tolerated systemically [43, 49]. This is usually not required in the treatment of native septic ankles. However, in FRIs requiring extensive debridement, the resultant 'dead space' lacks perfusion resulting in a low pH low oxygen tension environment ideal for bacterial proliferation despite systemic antibiotics. Additionally, in chronic infections (>4 to 6 weeks) and those requiring hardware retention with presumed antibiotic resistant biofilms, local supra-therapeutic doses of antibiotics up to 1000 times the minimum inhibitory concentration (MIC) improve sterilization of the wound [49].

We recommend use of high concentration antibiotic loaded PMMA beads or spacer depending on the size and shape of any bone defect. We prefer to make our own beads with high viscosity bone cement. At the first debridement, without organism identification, we will typically add 2 g of vancomycin and 2.4 g tobramycin powder. The powder is homogenously crushed with a blunt instrument such as the butt end of a Cobb elevator and mixed with the cement powder. The monomer is then added and mixed until a medium doughy texture is reached which may be workable into 5–7 mm beads. These are placed on a #1 polypropylene suture. The neutrophilic infiltration and the adhesive inflammatory exudate at the site of an infected wound can be significant complicating bead identification and retrieval. We find use of dyed bone cement or addition of a few drops of methylene blue dye aids in bead identifi-

cation. Additionally, after cement hardening and determining the number of beads that will fit in the wound, the suture is tied in a knot around the terminal beads to facilitate removal at the next washout (Fig. 3). With local antimicrobial use, consideration must be given to cytotoxic effects of different agents to osteoblasts, fibroblasts, and chondroblasts. Additionally, when used with polymethylmethacrylate (PMMA), the antimicrobial must be heat stable to up to 100 °C. A literature review and consensus paper from the Fracture Related Infections group found aminoglycosides and glycopeptides to both be heat stable with vancomycin, and tobramycin being least cytotoxic [49, 54]. Rifampin, doxycycline, penicillin, ciprofloxacin, and gentamicin produced significantly greater reduction in osteocyte activity, however in later rat in vivo models, gentamicin has not been found to impede fracture healing in infection treatment [54, 55].

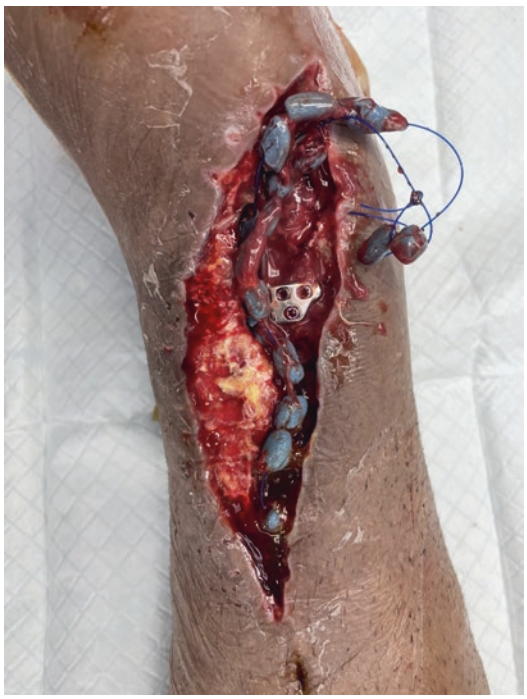

Fig. 3 Antibiotic polymethylmethacrylate beads on a prolene suture. Note the knot tied around the terminal bead, as well as methylene blue dye in the PMMA ensures retrieval of all beads after they have been in an inflamed wound

4.6 Soft Tissue

Preoperative planning should account for soft tissue coverage. Whenever possible, primary closure is preferable, but it must be tension free with the ability to evert skin edges as the inflamed skin will tend to invert. Suprafascial elevation and local flap advancement may be valuable techniques if the skin is healthy enough to tolerate. Avoid braided sutures as these may harbor microorganisms contributing to recurrent infection. Superficially, absorbable sutures should be avoided as they will instigate local inflammation in already compromised skin. Nylon suture is least reactive, and most tension free wounds can be closed with 3–0 vertical mattress sutures [48].

When adequate debridement will result in a soft tissue coverage defect, usually the distal third of the tibia and ankle area there may ultimately a need for a free tissue transfer for coverage [43]. There is limited data on the optimal timing of coverage. Single stage debridement and coverage of chronic osteomyelitis has been described, however this requires advanced coordination with plastic reconstructive surgeons or personal expertise in soft tissue transfers [56]. We typically perform serial debridements every 2–4 days until no further frank purulence is encountered. This is done in coordination with plastic reconstructive surgeons with the aim of definitively covering the wound either at the time of or within 3 days of the last "clean" debridement (Fig. 4). If the wound is going to require tissue transfer for coverage and requires multiple washouts, the wound should be managed with an antibiotic bead pouch. We fashion ours by making and inserting antibiotic cement beads as described above. The surrounding skin is cleaned of any residue with alcohol and then tincture of benzoin is applied to the skin. An occlusive adhesive such as Ioban™ 3M™ is then used to create an airtight seal. Finally, an 18G spinal needle and syringe is inserted from a remote location through the subcutaneous tissue into the wound, and the remaining air is aspirated from the bead pouch.

Some have described using negative pressure wound therapy (NPWT) dressings on wounds

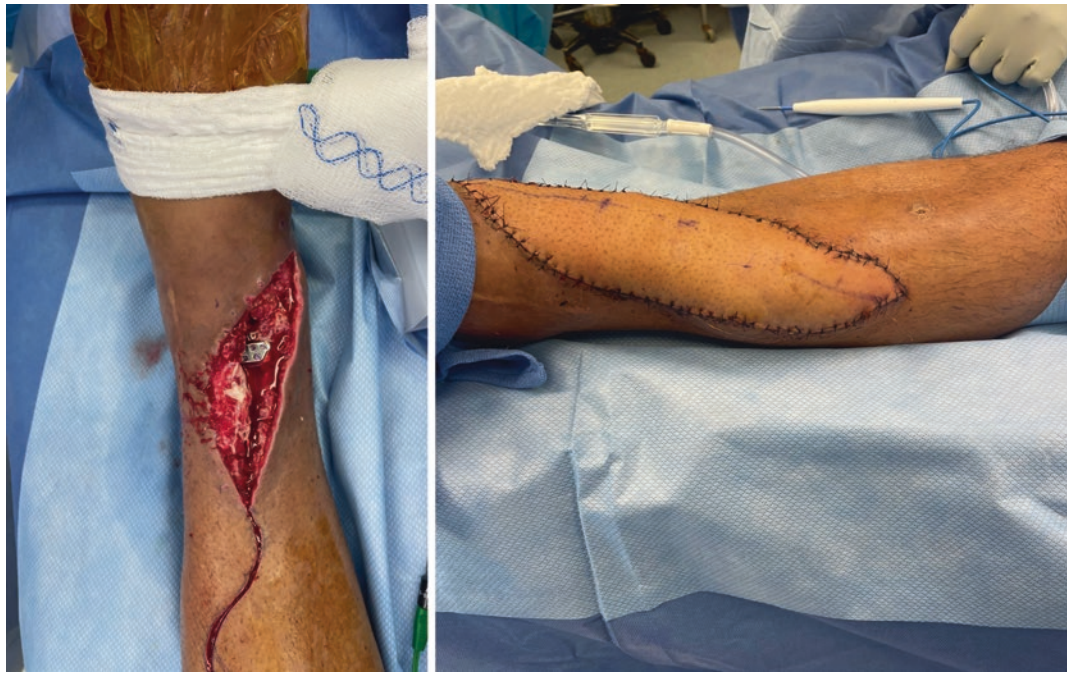

Fig. 4 Note healthy bleeding at all surfaces after two debridements with no further necrosis or purulence noted, at this time, due to the distal third of the tibia location of this soft tissue defect this patient underwent a free tissue transfer with an anterolateral thigh fasciocutaneous flap anastomosed to the anterior tibial artery

pending coverage. These have been shown to stabilize the wound environment, reduce edema, improve tissue perfusion, and stimulate beneficial cells at the wound surface [52]. This is an effective short-term tactic pending definitive coverage. However, in a frankly infected wound bed we prefer a bead pouch as NPWT sponges may lead to colonization with resistant organisms and possibly persistent infections [43, 57]. Some have proposed the use of surgical drains when dead space is present, however we are not aware of any studies evaluating the outcome of debridement with or without a surgical drain [3, 25, 48].

5 Overall Management/ Medical/Antibiotics

Management of antibiotics requires knowledge of the local antibiogram, resistance, patterns, as well as the common infecting organisms. Infecting organisms have been reported as *Staphylococcus aureus* in 54–65% of patients and oxacillin-resistant in 13–23% [16, 29]. Other organisms include staphylococcus epidermidis 23%, and the remainder were *Enterobacter cloacae*, *Propionibacterium acnes*, Acinetobacter, Serratia, *Pseudomonas aeruginosa*, and Vancomycin-resistant Enterococcus [16]. Ultimately, antibiotics should be tissue culture specific. Organism identification should not be based on any superficial or draining sinus tract swabs as these are often colonized and not representative of the underlying infection which may be sessile [42].

For native septic joints, antibiotics should be initially held until a sample is obtained such as through aspiration, but then empiric broad spectrum antibiotics covering both gram-positive and gram-negative organisms should be started expediently to reduce the ongoing damage of the infection in the joint. In postoperative infections, we recommend antibiotics be held prior to obtaining cultures unless the patient is exhibiting systemic signs of sepsis. After organism identification, therapy may be narrowed to lessen

side effects and reduce production of resistant organisms. Antibiotics typically are given for at least 6 weeks postoperatively for deep soft tissue and joint infections [25]. If hardware is being maintained for fracture healing, then antibiotics are continued until healing, debridement, and removal of hardware, and then generally continued for 6 weeks post hardware removal.

There is evidence that rifampin can have better penetration of sessile forms of staphylococcus than other antibiotics. In a randomized controlled trial of patients presenting with acute or subacute infections (less than 2 months of symptoms), involving Staphylococcus epidermidis or Staph aureus organisms, had stable implants at debridement, and able to tolerate long-term treatment (3–6 months) with a rifampin-ciprofloxacin protocol experienced a 2-year follow-up cure rate of 100% [58].

Ultimately the duration of antibiotic treatment should be individualized for each patient guided by clinical and laboratory evaluation. We recommend this be determined in conjunction with infectious disease consultants as they can weigh in on local microbial resistance patterns, cost considerations, adverse drug reactions, and interactions [3, 16]. The Fracture Related Infections (FRI) group has recommended patients with FRIs to be managed by a multidisciplinary group. Antibiotic stewardship programs with design for improving appropriate use of medications through the selection of antibiotic regimen, dosing, duration of therapy, and route of administration are recommended. Treatment of FRIs requires expertise in bone and soft tissue reconstruction, microbiology and local antibiograms, antibiotics effects and side effects, as well as advanced diagnostic imaging. Proposed members of such teams include infectious disease physicians, clinical pharmacists, local hospital infection control department, nurses, musculoskeletal radiologists, nuclear medicine specialists, and orthopaedic and plastic reconstructive surgeons [43]. Involvement of each of these may be guided on a case-by-case need. When such multidisciplinary approach is not feasible, consideration should be given to referring the patient to a center with more specialization and multidisciplinary capability for complex cases [43, 46].

6 Outcome

Following their protocol for hardware retention less than 10 weeks or removal after 10 weeks, Zalavras et al. reported complete infection clearance in 13/18 (72%) of patients with the remaining 5 experiencing recurrence. Four of these were in compromised hosts as described by Cierny-Mader [9, 16]. Three were in patients with hardware retention, and two of these were cleared of infection after repeat washout and hardware removal after fracture consolidation. An additional two patients had recurrence with instability due to hardware loosening and malreduction. These patients were in compromised hosts and ultimately underwent amputation to ultimately yield an amputation rate of 3/18 (17%). Two of these were in diabetic patients, however patients should be counselled that peri-implant infections about the ankle are serious infections and failed salvage may result amputation [16]. Additionally, smoking has been found to be an independent predictor of failure of treatment of fracture related infections, with an estimated risk of failure 3.7 times higher than nonsmokers [11].

In late presentations of FRI where bony union has occurred and debridement with hardware removal can be performed, there is a high rate of successful infection clearance. One study reported no recurrences in 14 patients for whom hardware could be removed at the time of debridement [16].

If infection has been going on for a prolonged time and involves the joint, it is unlikely the patient will have a good outcome maintaining the joint as there may be significant breakdown of the articular cartilage. However, reasonable results can be expected with a structured protocol for managing the infection followed by a talocrural fusion. Thordarson et al. reviewed 5 patients with septic arthritis presenting with average 8 months of infection and radiographic evidence of joint destruction and osteomyelitis. They were all treated with aggressive debridement, deep

biopsy, and targeted antibiotics, followed by a second debridement 3–5 days later and free flap coverage. After infection clearance and flap maturation, the patients underwent an ankle fusion at average 3.7 months after debridement and all went on to union at average 3.5 months. All patients were ambulatory without aid and satisfied with their outcome [59]. Another series reported 19 patients with chronic infections treated with aggressive I&D, hardware removal, antibiotic bead placement with gentamycin. On average, they underwent 2 washouts before free flap coverage (in 7/19 patients) and external fixator placement. After average 6 months, patients underwent arthrodesis at average 6 months with about a 50% union rate, in those who did not unite on initial treatment, they were repeat debrided and additional stability and bone graft added. Eighteen of 19 patients went on to stable union. The one patient with pseudarthrosis was a heavy smoker [60].

Given the recurrence risk after treatment of any infection, patients should be followed for a minimum 12 months after final therapy conclusion [43].

7 Conclusion

The treatment of infections about the ankle, especially postoperative fracture related infections is complex and requires a thorough and systematic approach for a successful outcome. The key recommendations in evaluation and treatment can be summarized as:

- Establish a diagnosis, with suggestive signs of infection mandating further investigation and prompt treatment. Diagnosis requires deep tissue sampling, not superficial swabs.
- Empiric broad-spectrum antibiotics should be started after obtaining culture samples and should be tailored to culture with a multidisciplinary approach.
- Stability is required in treatment of fracture related infections.
- Careful and thorough debridement is the mainstay of treatment and should not be compromised. When appropriate debridement results in defects, strategies should be employed for dead space management and vascularized soft tissue coverage.
- Low pressure irrigation should be used with enough volume to clean the surgical field and flow clear.
- Local high concentration of antibiotics should strongly be considered.
- Optimize the patients' health status through a multidisciplinary approach. Smoking cessation should be sought, metabolic factors corrected, nutritional deficiencies screened and improved, and weight reduction strategies.
- Multidisciplinary approach is beneficial and should be implemented in complex FRI cases. Consider transfer to a specialized center when a team approach or experience is lacking.
- Patients should be followed for a minimum of 1 year following definitive treatment of these infections.

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