Managing fracture-related infection

Asanka Wijendra
Jerry Tsang
Jamie Ferguson
Martin A McNally

Abstract

Fracture-related infection (FRI) is a serious complication that can result in poor outcomes, delayed bone-healing, soft tissue compromise, and prolonged hospitalization. FRI can present in various ways, largely depending on the timepoint after fracture. Management of this condition can be challenging. In this article we consider how to approach this condition and look at the rationale for decision-making in managing cases with complex infection.

Keywords Decision-making; excision; fracture-related infection; management; sampling; treatment

The problem

Fracture-related infections (FRI) have two concurrent and interrelated orthopaedic problems: 1) deep bone infection and 2) potential impairment of fracture healing.[1]

Infection can affect a fracture or its stabilizing implants at the time of surgery, at the time of open fracture, when wound cover is comprised, or rarely, following haematogenous spread. Once this occurs, bacteria can quickly establish a biofilm on implants or any devitalized fracture fragments. This biofilm confers massive protection from the immune system or systemic antibiotics. The resultant inflammation and/or further soft tissue stripping, caused by any subperiosteal abscess formation, can produce further compromise in bone viability and a hostile environment for ongoing bone healing. Once biofilm is established, systemic antibiotics alone cannot eradicate infection and surgery will be required. Surgery can be time critical. Early intervention with debridement, antibiotics and implant retention (DAIR) might control infection before implant stability is compromised. Once implants are loose, they usually need to be exchanged or removed.

Asanka Wijendra ***BSc MBBS MRCS*** *Specialty Registrar in Trauma and Orthopaedics, The Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, UK. Conflicts of interest: none declared.*

Jerry Tsang ***PhD FRCSEd(Tr & Orth)*** *Senior Fellow in Limb Reconstruction, The Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, UK. Conflicts of interest: none declared.*

Jamie Ferguson ***MB ChB(Hons) MEd FRCS(Tr & Orth)*** *Consultant in Limb Reconstruction, The Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, UK. Conflicts of interest: none declared.*

Martin A McNally ***MD FRCSEd FRCS(Orth)*** *Professor and Honorary Consultant in Limb Reconstruction Surgery, The Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, UK. Conflict of interest: none declared.*

The principles of managing fracture-related infection

The ultimate aim of FRI treatment is to achieve fracture consolidation and infection eradication. Whilst many similarities exist between FRI and prosthetic joint infection, one major difference is that fracture implants can be removed after bone healing, without loss of function. This raises the potential that suppression of infection until fracture union, with the later option of implant removal if required, can be a curative option in some cases.

The important components of FRI management include:[2]

1. Optimization of host factors and fracture healing potential
2. Microbiological diagnosis to guide antimicrobial therapy
3. Achieving fracture consolidation
4. Eradication of infection as the final outcome (this can sometime be achieved by initial infection suppression until union)
5. Healing of the soft tissue envelope
6. Restoration of function
7. Adequate ongoing follow-up to look for and treat signs of chronic infection/osteomyelitis.

In early FRI, when the fracture remains unhealed, the goal is to provide an environment that will support fracture healing. Outcomes can be improved by treating FRI patients within a multidisciplinary team environment.

Timing of intervention

It is not uncommon to encounter inflamed surgical wounds during the early postoperative period, creating a diagnostic dilemma for surgeons. Ultimately before considering surgical intervention, the surgeon must first suspect the diagnosis of infection. This has been made more straight forward since the FRI consensus statement which recognizes wound dehiscence, purulent discharge, or a new sinus as signs confirming infection.[3] However, patients may present with other signs that are not confirmatory, but rather 'suggestive' for infection (see Figure 1). These include wound redness, a fever, persistent or new onset wound discharge, radiographic signs, a new effusion in the presence of periarticular implants, or raised inflammatory markers. When present, these signs should prompt close observation or surgical intervention.

If any suggestive signs are present, without confirmatory signs, a short period of observation is reasonable to see how the symptoms evolve, providing the patient is systemically well. Some wounds may appear erythematous or leak for reasons other than deep infection. In these cases, the wounds would be expected to improve spontaneously over a few days.

The surgeon should reflect on the potential risks of surgical intervention balanced with the potential gains of undertaking early surgery. The advantage of addressing FRI at an early stage is that DAIR is more likely to be an option. However, early intervention on all cases risks morbidity associate with over treatment. For example, if a patient returns 2 weeks after ankle

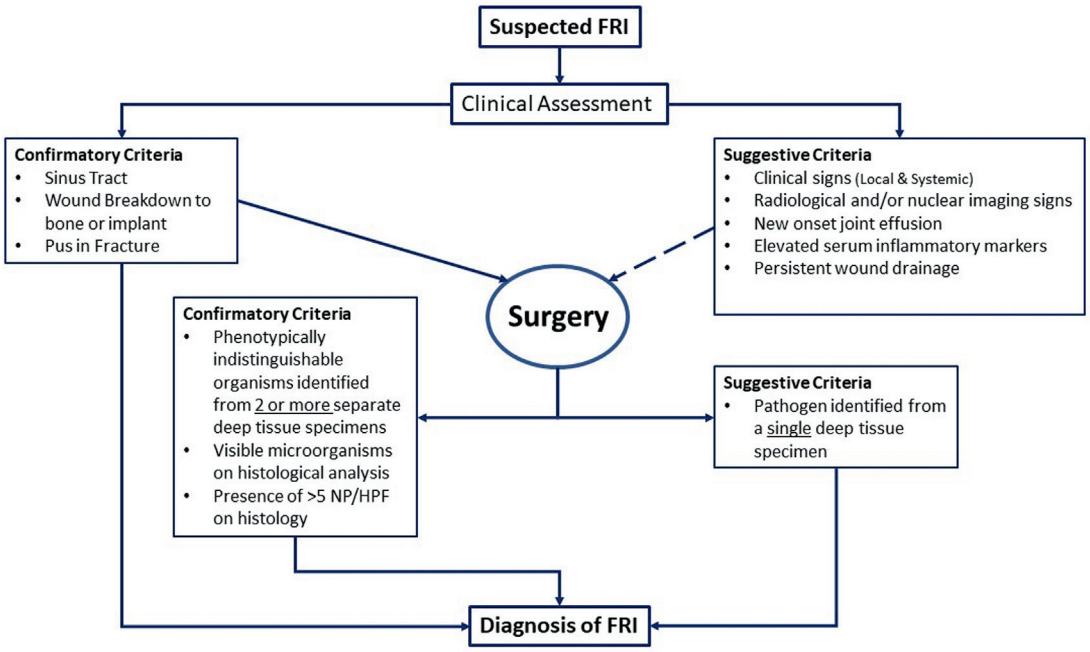

Figure 1 The International FRI Consensus Definition [3]. FRI, fracture-related infection; HPF, high-power field; NP, neutrophil polymorph. Adapted from reference 53.

fracture surgery with a red leaking wound, the risk of intervention at that stage is that the soft tissues will be impossible to close without a plastic surgical flap procedure to achieve wound closure. In this scenario, a short period of observation is acceptable to see if there is spontaneous improvement or if there is indeed a need for surgical intervention. Antibiotic treatment should not be given whilst further investigations are performed to confirm or refute the diagnosis of FRI. This is because it may be difficult to tell if an improvement on oral antibiotics is due to a self-limiting problem or is the result of a partially treated deep infection. By the time a wound becomes red or is leaking due to deep infection, it is unlikely that oral antibiotics alone will be sufficient in eradicating the established biofilm. Withholding antimicrobials before deep sampling will also improve the sensitivity of subsequent microbiological cultures.[4]

Historically, the duration of symptoms and time from fracture fixation were considered important factors to determine if implants could be retained. In theory the duration of infection symptoms is linked to the maturity of the biofilm and the potential for associated osteolysis and implant loosening. However, Metsemakers et al. were careful to emphasize that FRI should be viewed as a continuum with no clear threshold between late and delayed infections but still offer 10 weeks as a possible discriminating time point.[5] A rabbit model has demonstrated impaired fracture healing in infected osteotomes, with those remaining infected for up to 10 weeks having distinct histopathological changes not seen in the early infection group. The prolonged infection group demonstrated chronic inflammatory changes with fibrous encapsulation around the fracture site and sequestrum, plus evidence of peri-implant osteolysis.[6] A systematic review of clinical studies investigated the influence of time between fracture fixation and FRI surgery on outcomes.[7] The analysis included six studies involving 276 patients. Implant retention was associated with a successful outcome in 86–100% of patients if treated within 3 weeks, 82–89% when treated between 3 and 10 weeks and 67% when treated after 10 weeks. Due to heterogeneity of the data and low-quality studies, these results should be interpreted with caution.[8] DAIR is a reasonable treatment option for at least several weeks after infection presentation and this allows time to plan the surgical intervention and optimize patients preoperatively.

Preoperative optimization

While prompt intervention may be required, FRI often occurs in patients with complex local and systemic impairments.[9] As such, the patient should first undergo preoperative assessment, adequate investigation, and a multidisciplinary approach to host optimization.[5,9] This should include:

- Smoking and recreational drug cessation
- Correction of anaemia and vitamin D deficiencies
- Nutritional optimization
- Optimum diabetic control
- Lowering viral count in HIV-positive patients
- Psychosocial support with adequate housing conditions
- Stopping medications which may impair bone and soft tissue healing (such as steroids, non-steroidal anti-inflammatory agents, disease-modifying antirheumatic drugs)
- Ensuring optimized vascularity of the limb.

If possible, all antibiotics should be stopped for at least 2 weeks prior to surgery to optimize bacterial yields from cultures.[10] In the scenario where a patient presents acutely unwell and with evidence of sepsis, the condition is usually a result of a collection of pus, such as a peri-implant abscess or an adjacent septic arthritis. Blood cultures should be taken prior to administration of antibiotics and the patient should undergo urgent imaging and surgical decompression. Microbiological and

histological sampling can take place at the time of drainage. Definitive surgery can be delayed until a time when the patient is no longer septic. This allows time to carefully plan the definitive surgery.

Preoperative planning

There is no role for exploratory surgery in the definitive surgical management of FRI. Ensure adequate preoperative imaging has been obtained and that this has been studied to understand the likely extent of infection and to plan surgical approaches. MRI is very useful in determining the extent of osteomyelitis, but this is often unhelpful when implants are present, due to artifact.

Review of serial radiographs is often very useful to look for how the bone is responding over time. Living bone demonstrates periosteal reaction and can remodel. In contrast dead bone is unable to undergo disuse osteopenia so often appears relatively denser than the healthy surrounding bone. It will display no periosteal reaction, and its edges do not round off, giving the appearance of a fresh fracture line, even months after injury. Progressive lysis at a fracture is highly suggestive of infection (see Figure 2).

Careful attention should be paid to look for dead bone, under plates, as sequestra in fractures (see Figure 3), along the endosteum around intramedullary nails, or around old pin sites (so called ring sequestra) (see Figure 4). A targeted excision can then take place, preserving healthy bone, helping to maintain stability and facilitating fracture healing.

The principles of operative treatment

In managing FRI, the choice of intervention is influenced by the site of infection, the chronicity of the presentation, the degree of bone union, the pathogen type (if known), the integrity of the fixation, the condition of the soft tissues and any associated host comorbidities.

The important aims of definitive surgery include:

- Diagnostic sampling from deep tissue to establish the causative organism(s)
- Excision of necrotic or non-vital material and any implants not contributing to stability
- Management of residual osseous dead space
- Providing adequate osseous stability
- Achieving soft-tissue coverage to support bone healing and prevent the ongoing translocation of organisms into the fracture site
- Restoration of function.

There are a few options for treatment:

- DAIR procedure allows deep sampling to guide antibiotic therapy, a reduction in the bioburden and a potentially easier intervention before implant loosening and loss of fracture healing potential.
- Implant exchange: if the implant is loose or it is not possible to debride the implant (such as with an intramedullary nail) then the implant can be exchanged.
- Removal of loose implants and conversion to external fixation.
- Segmental resection of the infected fracture: if the fracture site is not viable then excision back to healthy bleeding bone may be required. Depending on the length of the segmental resection, a bone reconstruction technique may be required to manage the osseous defect.
- Close observation until union: if there is progressive bone healing, it may be appropriate to monitor the fracture until union, without surgical intervention. Once the bone has sufficiently healed to allow implant removal this can be undertaken (with or without plastic surgical soft tissue cover). This tactic is best employed when the patient is systemically well, when there is benefit in patient optimisation before surgery or when the infection presents late, close to fracture union.

As a general rule the surgeon should consider the most patient-friendly intervention with the quickest and most reproducible time to recovery. An early surgical intervention should be considered if it might avoid a more complicated problem later on.

For all of the strategies above, deep tissue sampling for both microbiology[11] and histology[12] using a systematic approach[13] and the delivery of systemic and/or local antibiotic therapy guided by culture results is routine.

There is controversy regarding the choice of fixation to achieve bone stability,[5] optimal delivery of local antibiotics,[14] and the methods required to reconstitute bone loss.[15] However, stability is an important element in successful outcome a well-fixed implant in an infected fracture confers greater benefit that the instability caused by its removal[16] (see Figure 5).

Debridement, antibiotics and implant retention

DAIR is indicated where there is a stable fixation construct with the potential to achieve fracture union, adequate soft tissue coverage, and the ability to administer systemic and/or local antimicrobial therapy.[17] A judicious debridement should be performed with the aim to remove all foci for potential ongoing infection, which includes but is not limited to haematoma, necrotic soft tissue, and non-viable bone. The aim is to excise non-vital tissue, rather than to excise all infected tissue. Well-vascularized tissues in a mechanically stable environment are able to deliver an immune response capable of clearing remaining infection.

A summary on the current state of collective understanding on FRI by Metsemakers et al. suggested that the following clinical factors should prompt consideration of implant removal and revision fixation: late presenting (>10 weeks since index surgery), intramedullary nail fixation, unstable fixation or inadequate fracture reduction, soft tissue compromise, host compromise, and resistant pathogen.[2] It should be noted that the authors emphasize that these are suggestive rather than absolute contraindications to DAIR. Furthermore, if the fracture is malreduced or the mechanical axis is poorly aligned then it is advisable to revise the fixation and exchange implants. With complex periarticular fractures, DAIR is often a more attractive option, as implant exchange is unlikely to provide as much stability as the original implants and joint surface reduction may be lost (see Table 1).

Previous intramedullary nail fixation is a relative contraindication to DAIR for FRI as the location of the implant precludes adequate debridement of the affected bone without removal of the hardware.[18] This is supported by two retrospective case series on outcomes of implant retention in FRI involving 162 patients that independently found the presence of an intramedullary nail to be a risk factor for failure of treatment.[19,20] Additional risk factors from these series were open fractures,[19]

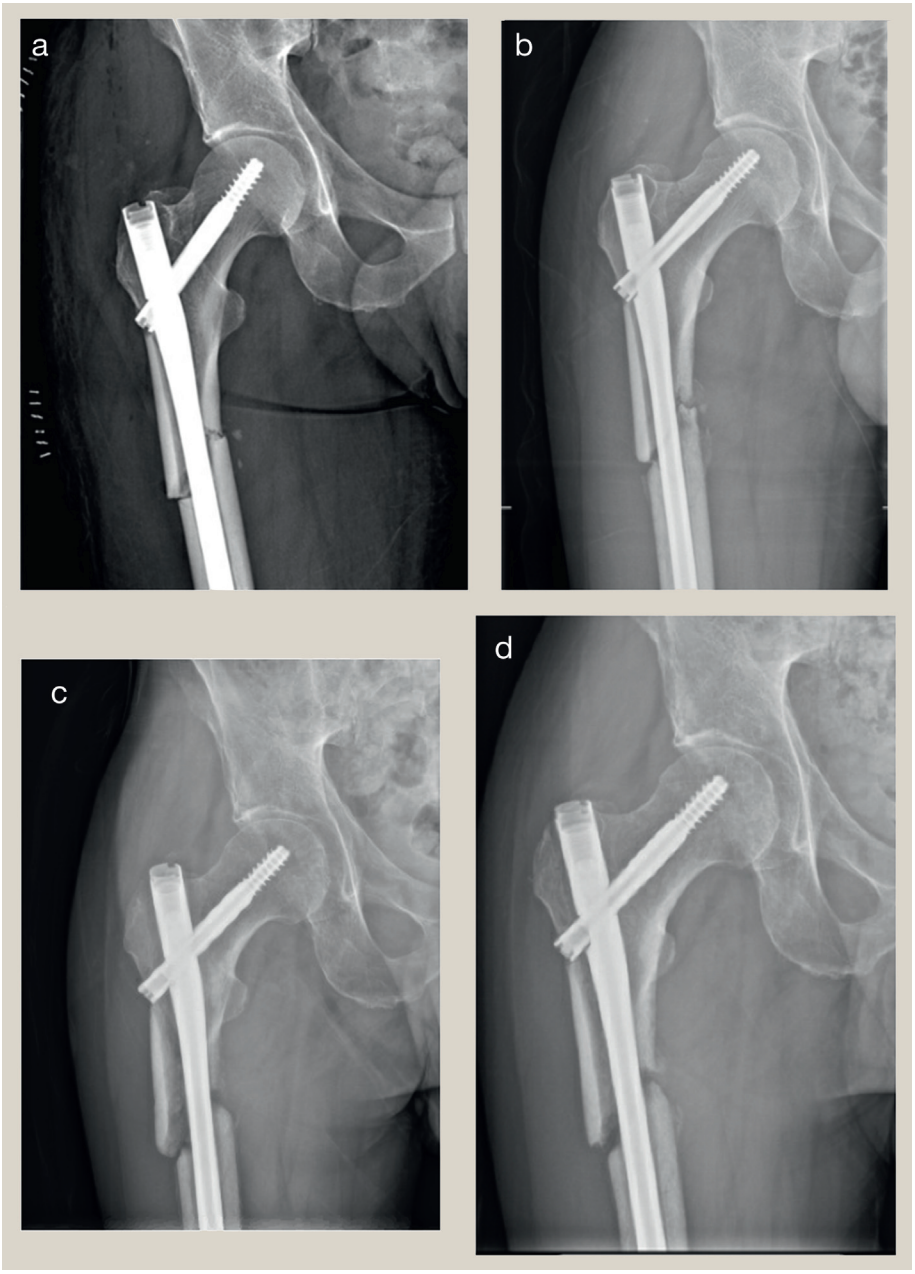

Figure 2 Closed right femoral fracture treated with an intramedullary nail. (**a**) Immediate postoperative X-ray demonstrates fracture acceptable apposition. (**b**) At 1 month later shows early lysis. (**c**) Taken at 3 months, showing further lysis and (**d**) at 6 months there is now lysis involving the medial cortex. This case was infected with pus in the canal on nail removal.

requirement for additional procedures to FRI and decreased initial injury severity score.[20]

There was strong consensus at the 2018 International Consensus Meeting, Philadelphia to support the removal of implanted hardware which is clinically or radiographically loose.[21] Consensus was based on the evidence from animal studies which demonstrated that the risk of FRI following internal fixation increased with unstable fixation in animal models.[16,22,23] However, it is important to acknowledge that the relationship between fracture instability and FRI, particularly when stability has been lost, may simply be a post hoc fallacy as it is more virulent infections that inhibit fracture healing which results in osteolysis and loss of stability within the fixation construct.[21]

Whilst the influence of soft tissue compromise on outcome has not been widely investigated in FRI, it has been shown to be of critical importance in the management of open fractures,[24,25] osteomyelitis,[26–28] and periprosthetic joint infections.[29,30] In a series of 433 FRIs, the addition of a soft tissue flap improved the success rate in tibial FRIs from 80% to 92%, compared to those without flaps.[31]

In a retrospective multicentre study of level one trauma centres that included 141 patients, Buijs et al. found that DAIR had a recurrence of 18% at a median follow-up 23 months, with 52%

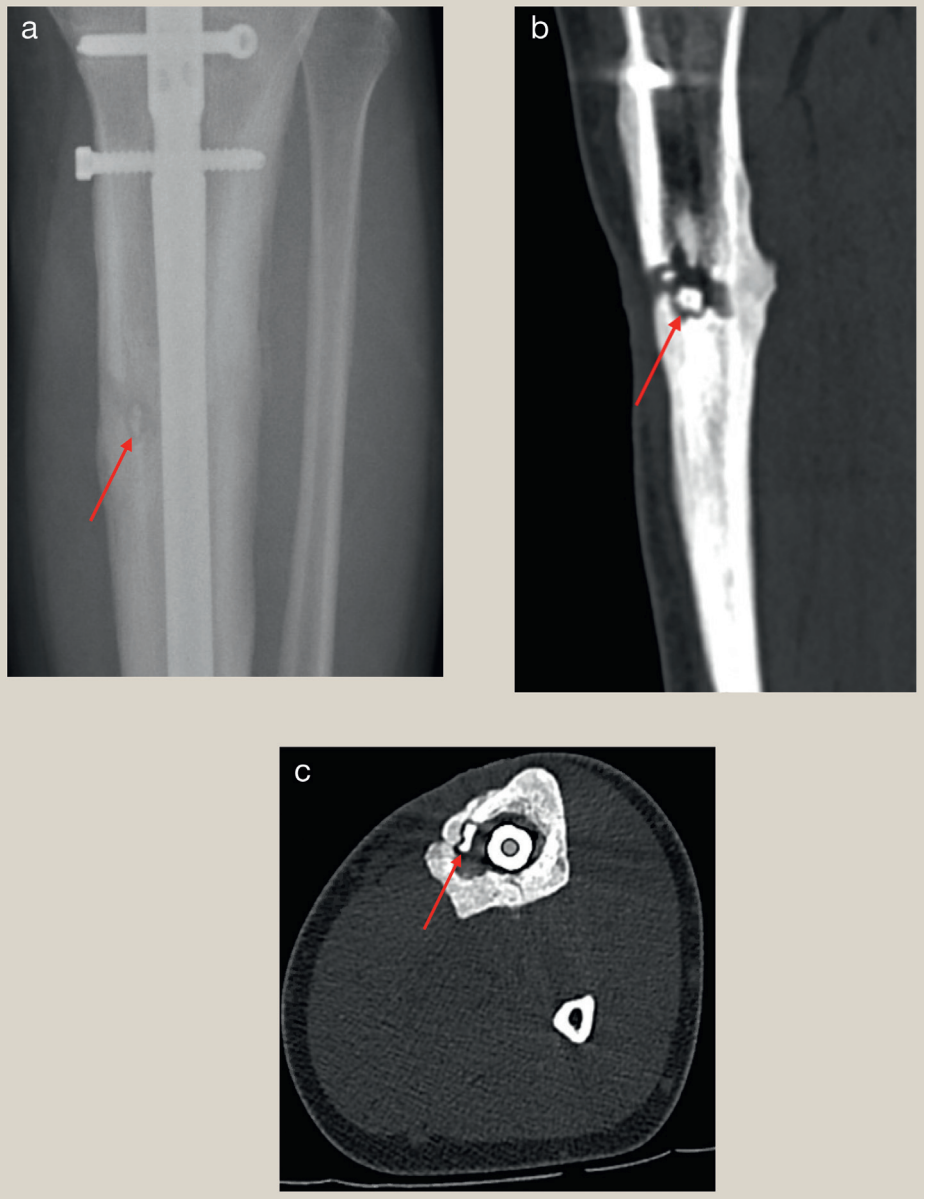

Figure 3 An 18-year-old patient with an infected tibial nail and sinus over the fracture site. (**a**) Antero-posterior X-ray with a sequestrum in the fracture site. (**b**, **c**) This sequestrum in the fracture site associated with a cloaca in the cortex.

of patients requiring at least two surgical procedures to control the initial infection.[20] McNally et al. showed that DAIR had a failure rate of 21.4%, while exchange to new internal fixation failed in 12.5%.[31]

Rightmire et al. evaluated the likelihood fracture union following DAIR for FRI in 69 patients.[32] Fracture union was achieved in 47/69 patients. Smoking was found to be the only independent risk factor for treatment failure. Fracture union was achieved at mean time 130 days. On average each case in the series underwent two debridement procedures.

Tissue sampling

Establishing the causative organism(s) is crucial for effective, targeted antimicrobial therapy following excision. To improve the accuracy and clinical value of these samples they should be representative of the site of infection and free from contaminant organisms. Skin swabs are of limited diagnostic utility and should not be relied upon for diagnosis.

Five tissue samples are taken from the site of suspected infection, ideally from the implant–bone interface. These typically consist of membrane around or beneath an implant, granulation tissue, periosteum, callus or bony sequestrum. Pus can also be aspirated and sent for culture. If too few samples are taken the sensitivity of culture decreases and if too many are taken, specificity decreases as the chance of culturing contaminants rises. A recent study showed that taking only three samples meant missing clinically relevant organisms in at least 1 in 10 cases.[11] Five samples are now widely accepted as a pragmatic balance between test accuracy and appropriate use of laboratory resource.[33]

To reduce risk of cross-contamination, the following should be undertaken:

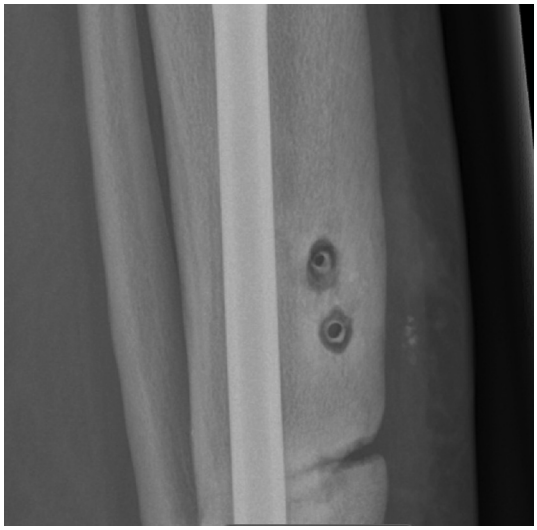

Figure 4 A radiograph showing two ring sequestra from a previously applied circular ring fixator. Note the osteolysis surrounding the necrotic ring of dead bone caused by heating of the bone during wire placement.

- The samples should be taken early into the surgical procedure
- Each sample should be collected with a no-touch technique using separate clean instruments for each individual microbiology sample (see Figures 6 and 7).
- The surgeon should avoid putting their fingers in the wound.
- Using suction should be minimized during sampling, to reduce pulling contaminants into the wound. A clean dry swab should be used each time an area of the surgical field needs to be dried to improve visualization.
- Any instrument can be used for sampling, such as, scalpels, forceps, curettes or synovectomy rongeurs, as long as the instrument has not been used in the operation until the time of sampling and the tip of the instrument has not been touched by the scrub team, surgeon, or patient's skin.

Histology can also provide valuable clinical information in the diagnosis of infection, especially if no organism(s) are cultured. It has been shown that in late FRI an infection can be definitively diagnosed if more than five polymorphonuclear cells per high-power field are detected; with the absence of any neutrophils diagnostic of an aseptic non-union.[12]

Sinus tracts should not be sent for culture. If the sinus has been present for more than 3 years we recommend this is sent for histology to exclude the rare possibility of a malignant transformation into a squamous cell carcinoma (Marjolin's ulcer).[35]

Samples should be sent immediately from the operating room to the laboratory for processing. The longer it takes from a sample being taken to reaching culture media, the less likely it is a sample will be grown.[33] Along with the samples the laboratory should be provided with all relevant clinical details including clinical history of the patient, previous antibiotic therapy, the anatomical location of the specimens and any suspicion for the presence of atypical organisms.

Once sampling has been completed empiric antibiotics can be given; or in the context of surgery under tourniquet, within 10 minutes of deflation. All instruments used during sampling can now be used for the remainder of the operation if required.

Tissue excision

Once sampling has been completed, the incision can be extended to allow for adequate visualisation and excision of tissue. However, care should be taken to avoid stripping of periosteum from healthy bone. This surgery is performed under tourniquet where possible, to ensure good visualization of the operative field.

The goal of excision is to remove all dead and poorly vascularized tissue which could harbour biofilm, impair wound healing and would not be adequately penetrated by systemic antibiotics. Tissue fields that may be contaminated but which remain well vascularized will be penetrated by systemic antimicrobial agents and so do not necessarily need to be resected. The goal is not to radically excise all infected or inflamed tissue, but rather remove devitalized material not contributing to fracture stability or healing.

Excision of devitalized tissue should not be limited by concerns of the creation of bony or soft tissue defects but on ensuring all non-viable tissues have been excised.

One of the clearest ways to identify living from dead bone is to examine for bleeding from the bone surface. Bone, which is alive will display punctate bleeding, known as the 'paprika sign'. This is visible even when a tourniquet is inflated. Dead bone often has a slightly yellowed hue and will display an almost porcelain appearance with no bleeding noted. When chiselling the bone, living bone will produce curled shavings (much like wood) whereas dead bone is hard and will splinter.

Implants

Fracture stability is critical for infection eradication.[9] In cases of implant retention (DAIR), all screws should be tested and if loose they must be removed. If ultimately the implant itself is no longer providing adequate structural stability, it too must be removed and an alternative method to ensure stability implemented. They may be in the form of implant exchange or external fixation.

Plate removal

If the decision is for removal of a plate, consider these specific intraoperative steps (see Figure 8):

- On surgical approach identify any membrane covering the plate and dissect this free from surrounding tissue, until all of the membrane and plate are visualized.
- Excise membrane completely, sending samples for microbiology and histology.
- Prior to removal of the plate, score around the plate down to bone with a scalpel. Once the plate is removed, this membrane/periosteal layer sat between the plate and bone (which is highly likely to be harbouring biofilm) can then be easily removed in its entirety.
- A chisel should then be used to remove any cortical bone that was lying underneath the plate until bleeding bone is encountered (the paprika sign).

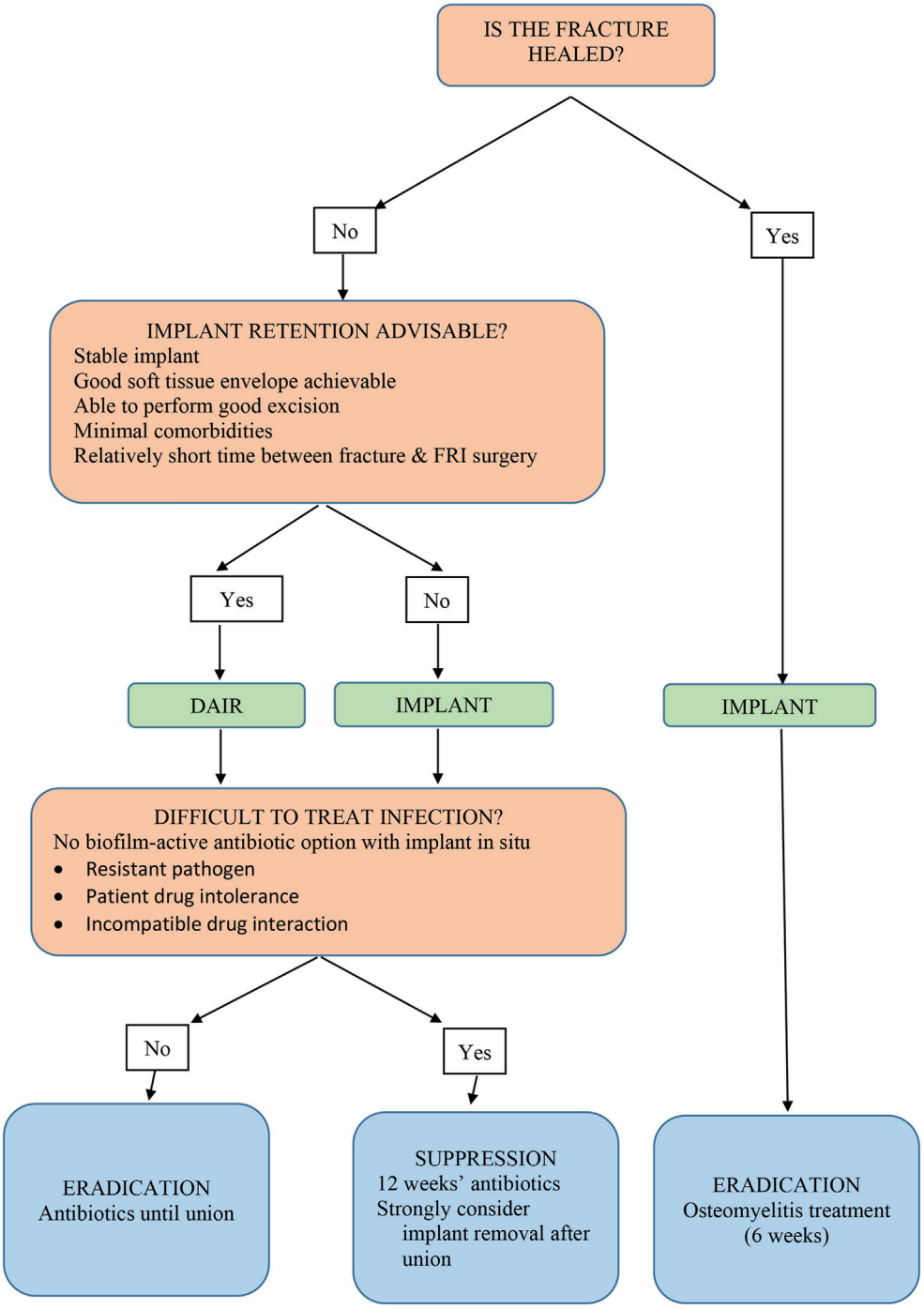

Figure 5 The surgical decision-making in fracture-related infection. Two key questions determine most of the surgical strategy: first, is the fracture healed? Second, is implant retention advisable? DAIR, debridement, antibiotics and implant retention; FRI, fracture-related infection. Modified from reference 9.

- All screw holes should be over drilled.
- Ensure adequate irrigation of the area.
- Fill all screw holes with an antibiotic carrier to both address the dead space and allow for local antibiotic delivery to the bone

Nail removal

If the decision is for removal of an intramedullary nail, consider these specific intraoperative steps:

- Excise any sinus tracts, tracking them down to possible bony cloaca – if any cloaca does exist, this needs to be adequately explored and debrided
- Remove the locking bolts and nail with appropriate extraction tools
- Ream the canal to ensure all endosteal biofilm has been removed
- Over-drill the locking bolt holes

Important factors to consider when weighing up the surgical options of debridement, antibiotics and implant retention (DAIR) versus implant exchange

Factors favouring implant exchange	Factors favouring DAIR
Fracture instability/implant loosening	Stable implant with no loosening
Fracture malreduction or mechanical axis malalignment	Complex periarticular fracture reconstruction (risk of increased instability with implant exchange)
Unable to perform good excision, e.g. intramedullary nail	Able to perform good excision
No progressive bone healing	Progressive signs of bone healing
Non-viable bone and/or fracture site lysis	Short time since fracture fixation
Long time since fracture fixation	

Table 1

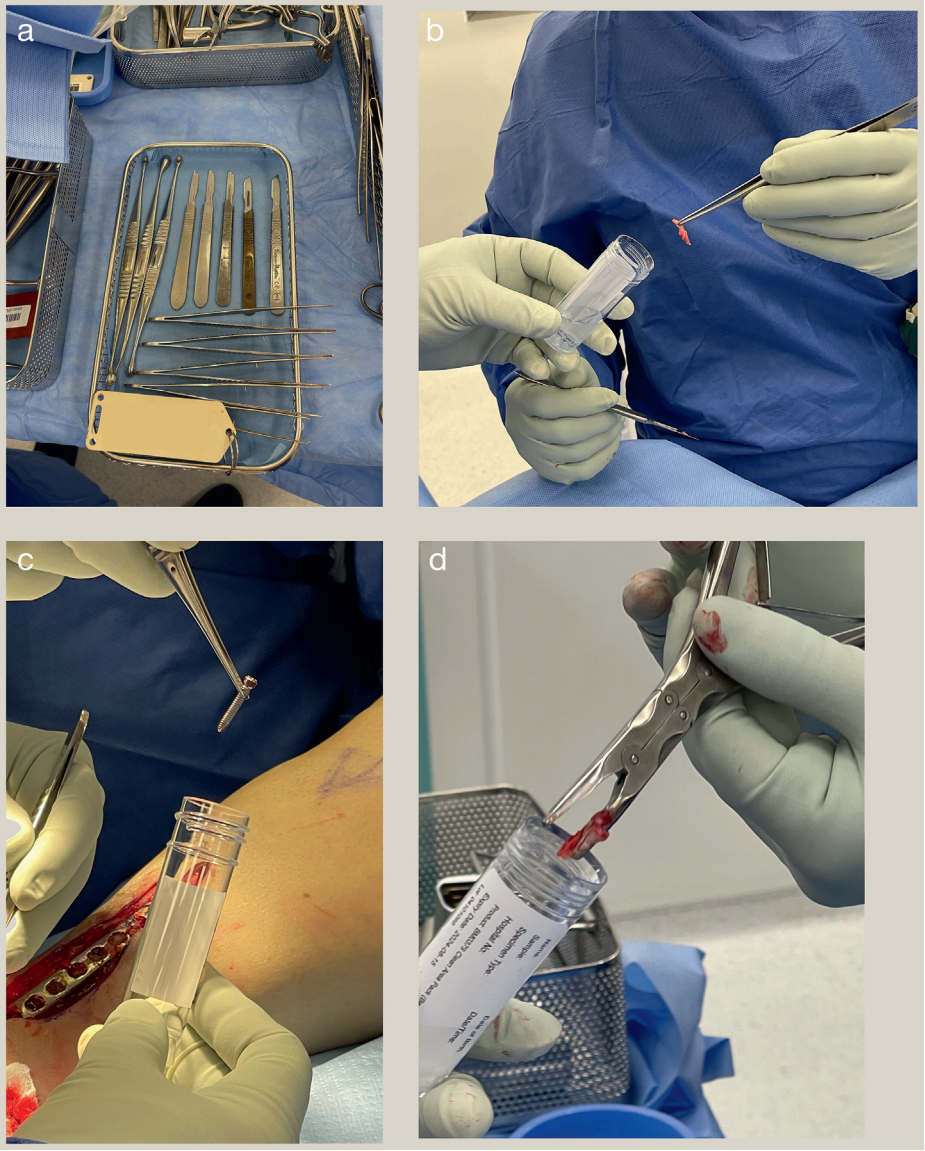

Figure 6 Microbiological and histological sampling. (**a**) A sampling tray containing separate instruments to take uncontaminated samples. (**b**) A tissue sample being collected with a careful no-touch technique. (**c**) Metalwork can be sent for sonication if required. (**d**) Any instrument can be used to sample as long it is clean and has not been used previously in the surgical procedure.

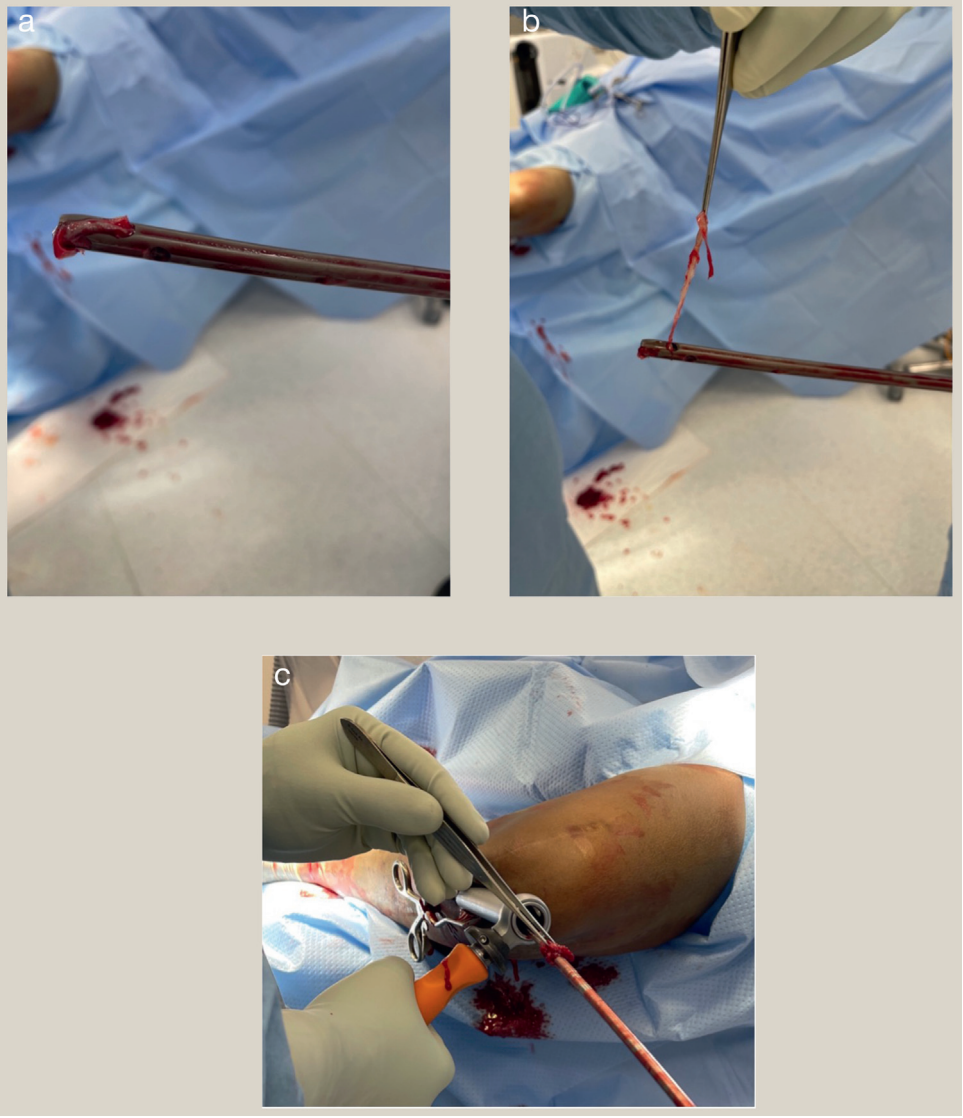

Figure 7 Samples can also be taken from around implants. The membrane around this tibial nail cannulation can be sent for microbiological sampling (**a**, **b**). Individual reamers can be used to collect samples of the endosteal bone for additional sampling (**c**).

- Any involucrum distal or proximal to the isthmus will not be adequately reached with a medullary reamer. In these cases, a separate window, often involving the locking bolt holes, can be created with a cooled drill and osteotome. Curettes and chisels can then be used to clear any remaining endosteal sequestrum
- Ensure thorough irrigation of the canal – an endotracheal suction catheter, fed into the canal from the entry point, can be used to ensure adequate delivery of the irrigation fluid.
- A local antibiotic carrier in pellet form can be used to address the dead space in the medullary canal. An endotracheal tube can be often of adequate aperture to help feed these pellets in via the nail entry point or cortical window (see Figure 9).
- A local antibiotic carrier can also be used to fill the defects from the locking bolt holes.

In recent years, there has been a vogue for the use of the reamer–irrigator–aspirator system (RIA) to excise intramedullary infections. There is no evidence that it removes any more biofilm, compared to standard sharp reamers and subsequent low-pressure washout with bladder syringes and suction catheters.

Irrigation

Following debridement, the area should be thoroughly irrigated to help reduce the bacterial load. A low-flow saline solution can be used for this with great effect as demonstrated by the FLOW trial.[34] In our centre we use a 0.05% aqueous chlorhexidine solution, which had a antibacterial action with minimal cytotoxic potential[10] but others have proposed acetic acid for possible anti-biofilm potential.[35]

Dead space management

There will invariably be residual planktonic bacteria in the surgical field following a through debridement and irrigation.[36] Any residual bone defects such as screw holes or defects in bone will fill with haematoma, acting as an ideal culture medium. Basic

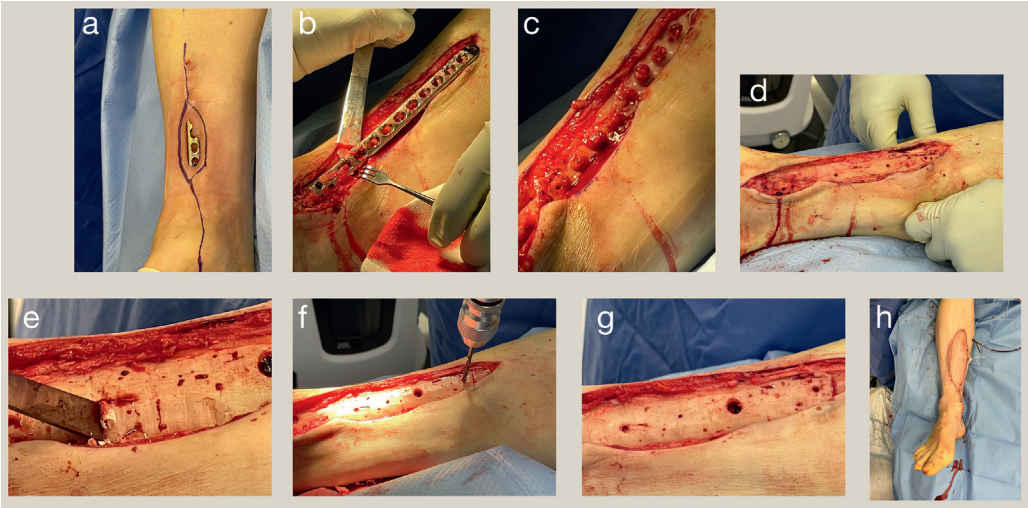

Figure 8 Plate removal for infection. (**a**) Exposed metalwork with underlying healed fracture. (**b**) Plate exposed and removed. (**c**) Membrane under plate sampled. (**d**) Dubious vascularity to bone after membrane removed. (**e**) Shows chisels used to excise back to healthy bleeding bone. Note abnormal bone splinters but normal bone rolls up like a wood shaving. (**f**) The old screw holes are over-drilled. (**g**) Normal paprika sign, even with the tourniquet inflated. (**h**) Following washout and dead space management with a dissolving local antibiotic carrier a free anterolateral thigh flap used to cover defect.

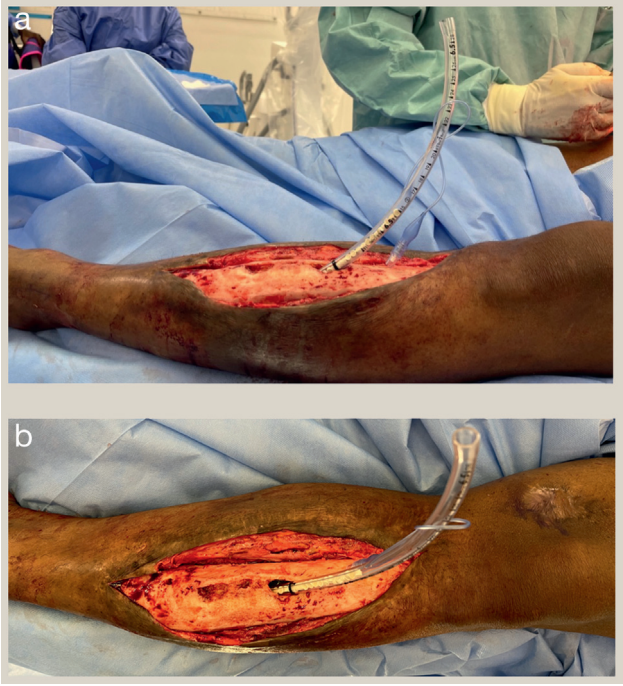

Figure 9 A case with tibial osteomyelitis with medullary canal involvement. Following sampling and bone excision the dead space is managed using local antibiotic carriers. The medullary canal can be filled with calcium sulphate pellets containing tobramycin with the help of an endotracheal tube to allow easy passage of these pellets.

science studies have demonstrated the ability of *Staphylococcus aureus* to reside within the canalicular system of healthy bone[37] and even intracellularly within osteocytes[38] and macrophages.[39] Systemic antibiotics alone may not be able to penetrate these areas,[2,40,41] risking re-colonization and biofilm reforming.

After excision, any osseous dead space can be filled using a local antibiotic carrier. This can achieve high concentrations of antibiotics at the site of infection, even when the local blood supply might be impaired, without adverse systemic effects. Traditionally, polymethylmethacrylate was used as the antibiotic delivery vehicle, but more recently biodegradable carriers made from ceramics such as calcium sulphate or hydroxyapatite have been used with the advantage of not having to be removed surgically. The most common local antibiotics include gentamicin, tobramycin, vancomycin and clindamycin. There is now increasing evidence that local antibiotics may improve the outcome of treatment of FRI, when combined with good debridement, stabilization and soft tissue cover.[42]

Soft-tissue closure

The integrity of the soft-tissue envelope is of crucial importance in the management of FRI. Not only does a well-vascularized envelope support bone healing, but the improved blood supply to the local area can deliver immune cells and systemic antibiotic therapy to the area of infection. Another very important function of wound closure is that it creates a sealed system to stop the ongoing translocation of organisms from the outside world, thus reducing the risk of selecting out resistant organisms.

There is little evidence to support the use of negative-pressure wound therapy in FRI. One study demonstrated that there was a twofold increase in infection recurrence with its use, often by delaying time to definitive soft tissue reconstruction.[43] Therefore, its use should be restricted to no more than a few days as a bridge to definitive wound closure.[21]

Involving a plastic surgeon in preoperative planning is invaluable as it can influence decision making and allow excision to proceed without fear of the subsequent reconstruction. This also allows single stage surgery for complex infection with quicker recovery of function.[44,45] Early coverage of infected fractures is key and more important than the type of flap used to achieve coverage, as long as it is robust.

Segmental bone reconstruction

All non-viable bone needs to be excised to treat infection and allow fracture healing. In some cases of FRI there is segmental bone loss. The optimal treatment option for these cases depends on the surgical expertise available. The defect size, defect location, state of the soft-tissue envelope and associated patient co-morbidities and functional state all have an impact on the treatment options.

The most frequently used methods to reconstruct segmental bone defect include the Ilizarov technique, the induced membrane technique, and free vascularized fibular grafting. A systematic review of critical-sized bone defects in FRI failed to draw clear conclusions on which techniques are better given the heterogeneity of the data.[46] These cases are recognized to be some of the most challenging to manage and are best done so in a multidisciplinary team setting.

Antibiotic therapy

Following surgery empiric broad-spectrum antibiotics can be started and rationalized as soon as culture results become available. Intravenous antibiotic regimes can be switched to oral options once cultures are available, assuming there were no positive blood cultures from a bacteraemia. The 2019 OVIVA study demonstrated that oral antibiotics were equally effective, as compared to intravenous antibiotics for the treatment of bone and joint infection in a group of 1054 patients.[47] If implants are retained biofilm active antibiotics may be considered if the cultured organism(s) are found to be susceptible. These include rifampicin, which is active against staphylococcal species and fluoroquinolones, such as ciprofloxacin, which is active against many Gram-negative organisms. Rifampicin should only be used in combination with another antibiotic, after surgical debridement and not started until the wound is dry to avoid the risk of developing resistant organisms. Antibiotic durations are controversial but as a general rule, if there are no retained implants following a thorough debridement, most centres would consider a 6-week course. If there is a retained implant 12 weeks may be considered.[9] If the bone has not healed some centres propose ongoing oral antibiotics until fracture union is achieved. This is because if the infection were to flare up after stopping antibiotics the surgical solution is likely to be more straight forward, involving implant removal without the need to consider skeletal stabilization.

Role of antibiotic suppression until union

Antimicrobial suppression has a role in one of two scenarios: 1) a Cierny–Mader type C host with no potential for optimization, or 2) to facilitate optimization of systemic or local biology, prior to treatment. Antimicrobial suppression for musculoskeletal infection has been previously advocated for patients in whom surgical intervention would constitute excessive risk, whether due to

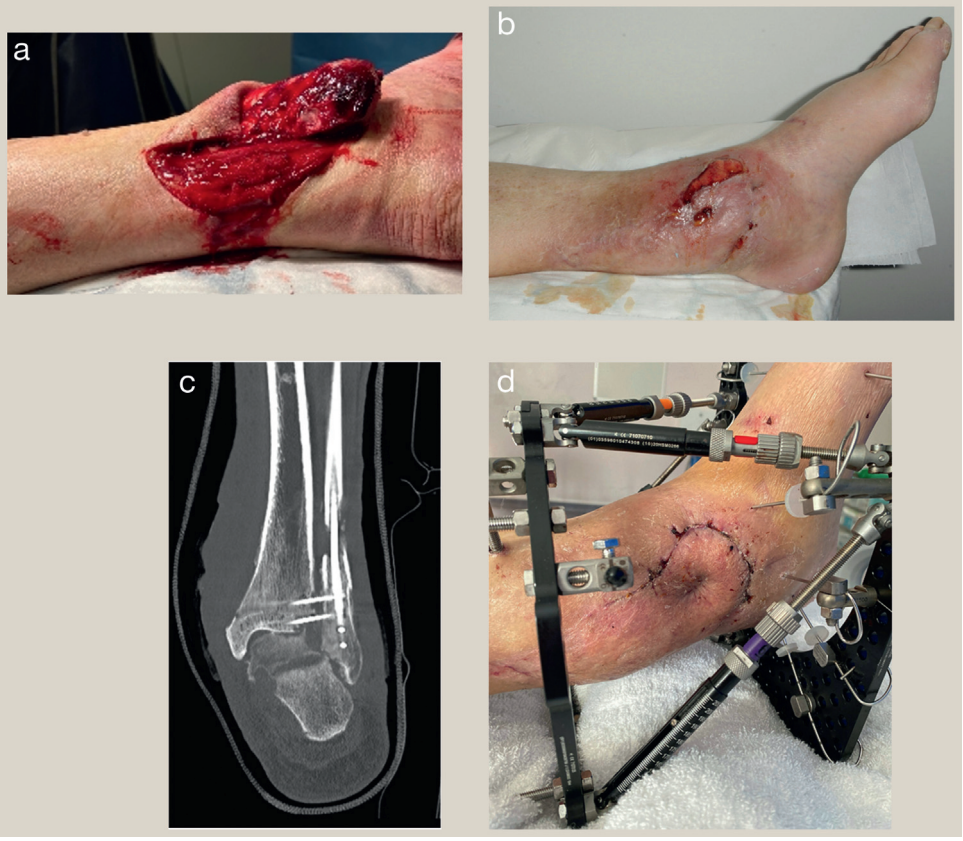

Figure 10 An example of using preoperative antibiotic suppression to make soft tissue reconstruction more straightforward. Open ankle fracture (**a**) treated with free gracilis muscle flap and fibula nail. Subsequent infection resulting in destruction of ankle and subtalar joints (**b**) Multiple draining sinuses developed around previous flap (**c**). Decision to undertake antibiotic suppression after ultrasound aspiration of ankle for culture to guide antibiotic choice. With antibiotic suppression the soft tissue envelope improved enough to allow an Ilizarov hindfoot fusion with reuse and advancement of old flap (**d**), thus avoiding the need for new free latissimus dorsi free flap.

physiological factors or patient preference in relation to symptom severity.

Preoperative optimization of host biology, both systemic and local (bone and soft tissue), has been shown to improve the outcomes of patients in the treatment of osteomyelitis.[27,48] In the presence of an acute localized exacerbation or episode of sepsis a short course of targeted antimicrobial therapy can be used to suppress symptoms whilst host biology is being optimized. Antimicrobial suppression can also be used to downstage both the soft tissue and bone components of FRI (see Figure 10). Marais et al. reported improved outcomes for patients in the treatment of osteomyelitis using an approach whereby local compromising factors such as cellulitis or an abscess, which may have previously prevented definitive surgery, were treated with culture-directed antimicrobials to facilitate a switch to a curative treatment pathway.[27]

With regards to the bone biology, antimicrobial suppression until fracture union can occasionally convert the situation from a Cierny–Mader anatomical type IV scenario (i.e. infection of the bone with segmental instability) into Cierny–Mader anatomical type I (medullary) or III (localized) infection which can be treated without the need for reconstruction of the bone. In both scenarios one converts the situation from a 'complex' infection to an 'uncomplicated' infection, as per the BACH classification of osteomyelitis,[49] which has also been shown to be associated with improved clinical and functional outcomes.[50]

Once again, pre-requisites for this approach are adequate control of strain across the fracture site to achieve union and adequate soft tissue integrity. The choice of suppressive agent should be based on either deep samples, such as an aspirate, or, empirically, using local pathogen resistance profiles.[4] The duration of suppressive therapy must be balanced against creating 'viable-but-culture-negative' infection.[51] A typical approach would be to withhold antibiotics for 2 weeks prior to surgery.

Follow-up

Patients should be reviewed regularly during treatment to identify problems early. If an external fixator is used, review every two weeks is recommended. Wound care may be needed more frequently. A minimum of 12 months' follow-up after surgery is advised to ensure there are no signs of recurrence, but most failures will present within 2 years of treatment.[52]

Conclusion

Managing FRI can be complex and requires a multidsciplinary team approach to achieve optimal patient outcomes. Early diagnosis can allow timely treatment which may avoid more complex issues later. The aim of treatment is to provide a supportive environment for fracture healing. This may include preoperative optimization to improve healing potential. The surgical tactics include implant retention, implant exchange, and implant removal. Osseous stability and achieving a competent soft-tissue envelope are two important factors in achieving the best outcomes. Preoperative planning is important to understand the likely extent of infection and to have the best chance of preventing infection recurrence. ◆

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