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GENERAL REVIEW

Current concepts in the prevention, diagnosis and treatment of fracture-related infection (FRI)

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Abstract
Fracture-related infection (FRI) is one of the most challenging complications following operative management of fractures. It can have profound implications for the patient, can be associated with considerable morbidity and often lead to impaired outcomes. There are significant healthcare-related costs. In recent years, there has been significant progress towards developing preventative strategies. Furthermore, diagnostic algorithms and management protocols have recently been reported. Lack of a strong evidence base has previously hindered efforts to implement these and develop established standards of care. There are multiple aspects of care that need to be considered and a multi-disciplinary approach is recommended. In this narrative review, we present the most up-to-date recommendations in the prevention, diagnosis and management of FRI.

Keywords Fracture · Infection · Osteomyelitis

Introduction

Infection following surgery with internal fixation of fractures is one of the most challenging complications in trauma and orthopaedic surgery. The incidence of infection following internal fixation for closed fractures has been reported to be 1–2% [1]. Historically, rates of infection as high as 50% have been reported for the most severe (Grade III Gustilo-Anderson) open fractures [2]. Despite advances in the management of these injuries, infection rates of up to 27% are still being reported, even in specialist trauma centres [3]. There is often the need for further operative management, prolonged admission, recovery and rehabilitation periods, need for long-term antibiotic administration and the potential for impaired outcomes and functional loss for the patient. A recent systematic review focussing on chronic and late-onset fracture-related infection (FRI) stated recurrence rates of up to 9% and amputation rates up to 5% [4]. There are many cases in which infection eradication may not be feasible necessitating chronic suppressive therapy.

Besides the potentially detrimental effects on patients, there are significant healthcare-related costs.

A recent comprehensive analysis of healthcare utilisation and related costs has demonstrated a 6.5-fold increase for tibia fracture fixation complicated by infection [5]. Increased length of stay and multiple procedures are often required with significantly increased costs reported [6, 7].

Despite the high incidence, the significant associated morbidity and the high healthcare-related costs, there has been limited progress in our understanding of the optimal management strategies. One of the main factors hampering our efforts to systematically evaluate data in this field has been the lack of consensus on a clear definition of fracture-related infection (FRI). The need for it has been identified for over 30 years [8]. A recent systematic review has further highlighted this, with only 2% of studies relating to the topic using a standardised definition of infection [9]. A recent international survey of trauma surgeons has echoed these findings [10]. Up until recently our approach to this spectrum of pathologies has been primarily guided by the principles set out for the management of osteomyelitis [11].

There has been extensive work on periprosthetic joint infections (PJIs) over the last years that has led to consensus definitions as well as established prevention and management pathways [12–14]. Despite both FRIs and PJIs

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addressing orthopaedic implant-associated infections, there are important differences that affect key aspects of diagnosis, prevention and management. Even though both conditions can manifest in a variety of clinical presentations and in different anatomical locations, in FRI further consideration is needed with regard to multiple fracture patterns, different degrees of soft tissue and bony injury and different patient conditions (poly vs. isolated trauma). Furthermore, the potential for implant removal following osseous union allows for different management approaches in FRI [15].

Definition

An expert multi-disciplinary group of scientific and medical organisations, with the support of the AO Foundation, was recently tasked with developing a consensus definition. In 2018, following a three phase consensus process (Delphi method), the group published their recommendations [16]. There was unanimous agreement that diagnostic criteria should be included in the definition of FRI. Following consideration of numerous clinical signs and diagnostic studies, the group defined two levels of certainty with regard to diagnostic features for FRI. Four confirmatory criteria were identified, and the presence of any one of them allows for definitive diagnosis of FRI to be established. Six suggestive criteria were identified whose presence may indicate infection and therefore mandates the need for further investigation to look for confirmatory criteria in order for a definitive diagnosis to be established. Table 1 provides a detailed description of the agreed confirmatory and suggestive criteria for the definition of FRI.

The group agreed that further classifications should be developed at a later phase to help establish treatment algorithms. In their most recent recommendations pertaining to the general treatment principles of FRI, the group highlighted the need for defining time intervals to differentiate between acute or chronic infection [17]. Further classifications according to location, mode of fixation, fracture stability, the presence of union, host type, soft tissue envelope and disease-causing pathogens will also need to be established [18].

Following initial recommendations from the expert group, a second consensus meeting took place in 2018 with further input from the AO foundation, the European Bone and Joint Infection Society, the Orthopaedic Trauma Association (OTA) and the PRO-Implant foundation. Following review of the most recent evidence, there was agreement in recommending two further diagnostic criteria.

Medical imaging modalities can provide important information in the diagnostic process. Each have their own advantages and disadvantages. Radiological signs had already been included as suggestive criteria. Nuclear imaging modalities such as white blood Cell (WBC) Scincitigraphy + single-photon emission CT (SPECT) or FDG-PET/CT have shown high diagnostic accuracy for FRI. However, they are not conclusive themselves and should therefore only be considered as a suggestive criterion for FRI in the consensus definition. With regard to histopathological findings, the value of histopathological criteria related to acute cell infiltrates (absent polymorphonuclear neutrophils [PMN]

Table 1 Diagnostic criteria for fracture-related infection (FRI) [16]

Diagnostic criteria for fracture-related infection (FRI)	
Confirmatory criteria	1. Fistula, sinus or wound breakdown (with communication to the bone or the implant)
	2. Purulent drainage from the wound or presence of pus during surgery
	3. Phenotypically indistinguishable pathogens identified by culture from at least 2 separate deep tissue/implant (including sonication fluid) specimens taken during an operative intervention. In case of tissue, multiple specimens (≥ 3) should be taken, each with clean instruments (not superficial or sinus tract swabs). In cases of joint effusion, arising in a joint adjacent to a fractured bone, fluid samples obtained by sterile puncture may be included as a single sample
	4. The presence of microorganisms in deep tissue taken during an operative intervention, as confirmed by histopathological examination using specific staining techniques for bacteria or fungi
Suggestive criteria	1. Clinical signs: pain without weight bearing or increasing over time or new-onset; local redness; local swelling; increased local temperature; and fever ≥ 38.3 C
	2. Radiological signs: bone lysis at the fracture site or around the implant, implant loosening, sequestration occurring over time, failure of progression of bone healing, periosteal bone formation at localizations other than the fracture site or in cases of a consolidated fracture
	3. A pathogenic organism identified by culture from a single deep tissue/implant specimen taken during an operative intervention
	4. Elevated serum inflammatory markers (a secondary rise after an initial decrease following trauma or a consistent elevation over a period in time): erythrocyte sedimentation rate, white blood cell count, C-reactive protein
	5. Persistent, increasing or new-onset wound drainage, beyond the first few post-operative days
	6. New-onset joint effusion in patients with an intra-articular fracture or when an implant penetrates the joint capsule

versus > 5 PMNs per high-power field [HPF]) has also been established for chronic/late-onset cases (i.e., fracture non-union) and should also be considered a confirmatory criterion in the consensus [19].

Prevention

Despite the extensive recent work that has focussed on the definition and management of FRI, the optimal strategies in prevention are still not established [20]. Guidelines to reduce the incidence of surgical site infection (SSI) in musculoskeletal trauma have been developed by the World Health Organisation (WHO) and the US National Institutes of Health Centres for Disease Control and Prevention (CDC) [21, 22]. The majority of those recommendations have been extrapolated from research not directly addressing musculoskeletal trauma. Similar to the management of established FRI, there should be a multi-disciplinary approach addressing all aspects of pre-, peri- and post-operative care.

Pre-operative care

Host-related risk factors including age, co-morbidities, malnutrition, medication history, smoking and alcohol consumption have been shown to correlate with the risk of infection in orthopaedic surgery and strategies to eliminate or modify them should be employed when possible [23]. This involves input from different specialties from the time of hospital admission to the time of discharge. The majority of these risk factors are long standing and therefore may not be reversible in the context of an acute trauma admission.

Screening and de-colonisation protocols for Staph.Aureus are commonly employed in elective orthopaedic procedures. Even though this may not always be feasible in the context of acute presentations with fractures, effort should be made to employ screening, especially if surgery is delayed or delivered in an ambulatory setting [24].

Peri and post-operative care

Operating room and personnel sterility

Trauma procedures with implants should be ideally be performed in orthopaedic dedicated theatres with clean areas for implant storage, and minimal personnel movement [25]. There is debate with regard to the effects on SSI and FRI rates when using lamina flow ventilation systems in the context of trauma [20]. Use of meticulous hand hygiene techniques by all members of the surgical team is important. Current recommendations support the use of alcohol-based solutions complying to a recommended hand-washing technique of no less than 90 s duration [26]. Appropriate surgical attire should always be worn and changed when visibly soiled [27]. Use of face masks is strongly recommended despite the fact that their effect in SSI reduction remains unknown due to the protection offered to the operating personnel [28]. Despite the lack of robust evidence, the use of double gloving technique is also recommended due to the documented high rates of perforation and contamination in orthopaedic surgery [29].

Surgical site preparation

Routine hair removal prior to trauma surgery is discouraged as it has been shown to be associated with increased prevalence of SSI. If necessary it should be performed outside the operating room using clippers [30]. Pre-operative site-specific washing with soap is encouraged as it has been shown to reduce the bacterial load [22].

The three main antiseptics most commonly used in the operating room (OR) for skin preparation include chlorhexidine, iodine, alcohol-based solutions or a combination, each with unique properties. Aqueous chlorhexidine can have both bactericidal and bacteriostatic effects. At low concentrations, it provides excellent cover against gram-positive bacteria and at higher concentrations good cover against gram-negative bacteria, viruses and fungi. This is offset by the potential for membrane disruption and cell death at high concentrations. It is often used in combination with alcohol which brings about a more rapid onset and longer duration of action. The addition of alcohol increases the risk of flammability, and therefore, meticulous drying is required. The cost is also significantly increased for alcoholic solutions. The most commonly used iodine solution is povidone-iodine. Iodine has bactericidal properties with good coverage against both gram-positive and negative bacteria,fungi and viruses. Povidone works by increasing the duration of action of iodine. Alcohol-containing iodine solutions are available with similar advantages and disadvantages from the addition of alcohol as in chlorhexidine solutions. Even though previous reports have recommended the use of alcoholic chlorhexidine, the majority have compared it to an aqueous-based iodine solution [31].

A recent review of skin antiseptics used in elective orthopaedic surgery has not found strong evidence to recommend one over the other and has also highlighted the importance of different anatomical areas with unique microbiota and response to antiseptics [32]. A recent prospective RCT has demonstrated reduced SSI rates in joint arthroplasty surgery by repeat skin preparation after draping [33]. A recent Cochrane review has reported lack of evidence for plastic adhesive iodine impregnated drapes to reduce the incidence of infection and in fact concerns have been raised that it may even lead to an increase [34].

Antibiotic prophylaxis

The routine use of a single dose broad spectrum antibiotic like a first or second generation cephalosporin has been shown to reduce the incidence of infection following internal fixation of closed fractures. It should be administered within 15–60 min before incision and a repeat dose given if the timing of surgery exceeds 2.5 h. The choice should always be considered based on local and host factors [35].

With regard to open fractures, current British Orthopaedic Association (BOA) / British association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) guidelines recommend that at the time of first debridement, co-amoxiclav (1.2 g) or a cephalosporin (such as cefuroxime 1.5 g) and gentamicin (1.5 mg/kg) should be administered, and co-amoxiclav/cephalosporin continued until soft tissue closure or for a maximum of 72 h, whichever is sooner. Gentamicin 1.5 mg/kg and either vancomycin 1 g or teicoplanin 800 mg should be given on induction of anaesthesia at the time of skeletal stabilization and definitive soft tissue closure. These should not be continued post-operatively. The vancomycin infusion should be started at least 90 min prior to surgery. Patients with anaphylaxis to penicillin should receive clindamycin (600 mg IV 6 hourly preoperatively) in place of co-amoxiclav/cephalosporin. For those with lesser allergic reactions, a cephalosporin is considered to be safe and is the agent of choice [36].

Recent systematic reviews have supported the early administration of first generation cephalosporins in all patients with open fractures [37, 38]. A recent review has concluded that there is currently insufficient data to support routine prophylaxis with aminoglycosides in all open fractures [39]. Although relatively safe in patients without risk factors, their use in the setting of polytrauma and hypotension leads to increased risk of nephrotoxicity [40]. Recent retrospective review from a Level 1 trauma centre demonstrated no statistical significant difference in rates of SSI when comparing use of 1st generation cephalosporin + aminoglycoside with use of piperacillin/tazobactam in Type 3 open fractures [41]. The timing of administration is crucial as delayed administration has been shown to increase the incidence of infection [42]. Current evidence does not support the use of prolonged courses [38]. It is important to bear in mind that the only randomised double-blind prospective study on the duration of antibiotic administration in open fractures supports this and dates back to 1988 [43].

There have been multiple reports recently on the use of local antibiotics. The proposed advantage of allowing for a constant delivery of higher concentrations in local tissues even in the presence of impaired circulation following injury is promising. Furthermore, their presence may help in reducing biofilm formation and colonisation [44, 45]. A meta-analysis of 2738 patients given local antibiotics in addition to systemic antibiotics for open fracture treatment showed a risk reduction of FRI of 11.9% when using combination treatment [46]. Despite the promising data been reported, there is still no consensus on their use and lack of clearly defined indications and dosing regime [47]. Antibiotic-coated intramedullary nails provide osseous stability whilst allowing for local delivery of antibiotics. Despite favourable outcomes been reported in severe open fractures [48], a recent systematic review has highlighted the need for further evidence to consolidate these findings [49].

Surgical debridement

Historical recommendations for the need for emergent debridement of open fractures have been challenged in recent years. Time to debridement is currently regarded as independent of infection risk if performed within 24 h provided there is no gross contamination [17]. This is also reflected in current BOA/BAPRAS guidelines. Thorough debridement of all devitalised tissue and meticulous handling of all injured tissue is required during the process of debridement. The use of low flow normal saline has been shown by the FLOW trial to be optimal for irrigation [50].

Wound care

In terms of primary wound closure technique in orthopaedic surgery, no difference has been shown between the use of staples or skin sutures [51]. There is currently insufficient evidence to provide strong recommendations on the use and duration of optimal dressings as well as with regard early (< 48hrs) vs delayed (> 48hrs) removal for inspection [20]. For severe open fractures with extensive soft tissue damage, evidence supports early tissue coverage by plastic surgeons using flaps [52]. Historically, the use of negative pressure wound therapy (NPWT) as an interim measure until definitive closure was advocated. However, more recently, the WOLLF trial has questioned this concept [53].

Diagnostic approach

As already mentioned, definitive and suggestive criteria for the diagnosis of FRI have been proposed [16]. While there are several clinical signs associated with FRI, there are two definitive criteria for diagnosing FRI: wound breakdown and purulent discharge around the fracture or the implant. All other diagnostic criteria like pain, heat, redness, swelling, etc., are considered suggestive of infection but not pathognomonic for it. The presence of these signs and symptoms should alert the clinician that further investigations are warranted to establish the cause.

Following initial history taking and clinical examination, baseline investigations are routinely performed. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white cell count (WCC) (specifically the Neutrophil count) are the most commonly conducted serology tests in orthopaedics when assessing for the presence of infection. The rise in these markers above the normal range is non-specific, and for this reason, these are considered suggestive and not diagnostic of infection [54]. A meta-analysis found limited value of the 3 markers individually and this is further complicated by the having different measuring protocols and devices [19].

With regard to imaging modalities, plain radiography remains the first choice of investigation even when FRI is suspected. While its diagnostic value is undefined it provides valuable information on the local bone, healing process, metalwork status and it is widely available, cheap and quick to attain. CT and MRI are the next line investigations with CT preferred to localize bony pathologies like the presence of sequestrum and MRI to ascertain extent of concomitant soft tissue involvement. However, it is nuclear imaging that is starting to play a greater role in FRI management. Nuclear imaging mainly consists of WBC scintigraphy and/or FDG-PET. The recent development of hybrid imaging including these modalities and CT/MRI allows for better anatomic detail. Both have displayed encouraging sensitivity and specificity in recent times but have their own limitations. WBC scintigraphy is laborious and time consuming and less accurate in the axial skeleton. FDG-PET is slightly less accurate and should not be used within the first month following surgery. In essence, none of the tests are yet conclusive and findings from imaging modalities are currently only considered as suggestive for the presence of infection [19].

As already discussed, regular laboratory and imaging modalities are useful and can suggest FRI but their findings are often equivocal. Hence, the gold standard remains the confirmed presence of a pathogen in deep tissue samples obtained during surgery. The literature has long had consensus that multiple samples were needed but until recently there was no method described to obtain them and as a result ad-hoc sampling was often done.

The current recommended sampling protocol has been extrapolated from the one developed for prosthetic joint infections and found promising results [55]. It is recommended that at least five deep tissue or fluid samples are obtained from the area of interest. Swabs, superficial or skin tissue and fluid samples are not recommended. [56, 57] It is also noted that multiple relevant tissue sampling, avoidance of antibiotics and better information provision on request forms lead to significant improvement in the detection rates of organisms [55]. The culture of a distinct organism from at least two samples is currently considered confirmatory for the diagnosis of a FRI [16]. However, even one positive sample can often be considered positive for infection in case of highly virulent organisms [12].

The antibiotic sensitivities of the organism will guide the choice of antimicrobial treatment. These can sometimes be slow to grow by being incorporated in a biofilm or be present in low numbers requiring extended cultures or enrichment cultures. Pre-culture antibiotics can interfere with the identification of the organism by inhibiting their growth on the culture, and therefore, antibiotics should be stopped two weeks before the sampling [55].

It is recommended that at the time of sampling, tissues should also be send for histological examination. Morgenstern et al. (2018) proposed that the presence of > 5 NPs/HPF had a positive predictive value for infected non-union of 100% and complete absence almost always indicates aseptic non-union. They concluded that using this histological criterion along with clinical signs and cultures resulted in diagnostic accuracy of almost 97% [58].

The use of rapid diagnostic techniques like a polymerase chain reaction (PCR) test is recognized in the pathology of PJI but like histology, its role in the field of FRI is yet unexplored. They offer the obvious advantage of being able to provide a diagnosis based on the ability to amplify and recognize the presence of sequences of DNA in samples. A recent study [59] on the use of multiplex PCR on sonication fluid found results comparable to tissue culture results. In conclusion, while the initial evidence is encouraging, data are scarce and more research is warranted for PCR to become a regular diagnostic criterion for FRI.

Management of FRI

The general treatment principles of fracture-related infection (FRI) consist of patient optimisation, bone and soft tissue debridement with defect management, local and systemic antibiotics and skeletal stabilisation. These are complex patients often with multiple previous operations and additional co-morbidities, and so should be managed in a multidisciplinary team setting.

Patient optimisation

As previously discussed in prevention of FRI, patients with significant co-morbidities have poorer outcomes after trauma and fracture treatment [16]. In treating FRI, especially in the chronic form, the patient and affected limb should be medically optimised as much as possible prior to starting treatment. Nutrition, anaemia, obesity, depression, alcohol abuse and smoking are all known to be associated with increased surgical complications and/or surgical site infections and should be reviewed and management strategies commenced.

The treatment of cardiovascular, pulmonary, renal and endocrine disorders (including thyroid function and low vitamin D) should also be optimised prior to surgery [1]. The management of diabetes is especially important as post-operative lengths of stay are known to increase as the Hb1Ac increases [60]. Finally, the vasculature of the affected limb should also be reviewed and attempts to improve should be undertaken where necessary.

Surgical management

In acute (< 6 weeks post-surgery) or chronic (> 6 weeks) infection, the mainstay of management is surgical debridement of the skin, soft tissue and bone to remove and sample infected tissue followed by treatment to heal the fracture and provide soft tissue coverage. Implant retention, removal or exchange depend on fracture union, fracture reduction, implant stability/loosening and chronicity of infection. It is considered reasonable for acute FRI to be treated with debridement, antibiotics and implant retention (DAIR) until fracture union occurs provided that there is a stable osteosynthetic construct, a vital soft tissue envelope, no major local or systemic impaired host physiology, an identified susceptible pathogen and a situation allowing for proper debridement to reduce bacterial load [17, 61]. A recent systematic review was performed to establish safe time intervals for DAIR. The authors were unable to establish these and could not conduct a meta-analysis due to the heterogeneity of the available literature [62].

Bone and soft tissue debridement

Meticulous debridement of non-viable and infected soft tissue should be undertaken by a surgeon with necessary experience and in collaboration with a plastic surgeon. It is important that debridement is not compromised over fears of future soft tissue coverage. Negative pressure wound therapy (NPWT) can be used to bridge the timeframe between initial debridement and plastic surgical coverage. However, this should be used for days rather than weeks due to the significant bacterial colonisation that has been shown to occur in wounds treated with long-term NPWT [63]. Other techniques such as the application of antibiotic-loaded cement bead pouch dressing may be employed. Definitive skin coverage should be guided by plastic surgeons and the characteristics of the defect, with no significant difference in union or infection found between muscle and fasciocutaneous flaps [64].

Infected bone should be resected to a level where uniform punctate bleeding bone (the paprika sign) is seen. Preoperative imaging will also act as a guide as to the extent of infected bone. In terms of the margin of excision, Simpson et al. found that a ≥ 5 mm resection margin led to no recurrences of chronic osteomyelitis. However, in Cierny Type A hosts, there were no recurrences in those that had a marginal resection of < 5 mm. Therefore, bony resection can be tailored to the patient [65].

Thorough irrigation should follow debridement to further remove dead tissue and reduce the bacterial load. As previously mentioned, the FLOW trial showed no difference in infection when irrigating open fractures with high versus low pressure lavage and found saline superior to soap [50].

Bone defect management

After adequate debridement, it is common for 'dead space' to be formed due to the absence of bone. This space should ideally be filled with a substance that delivers local antibiotics and allows bone growth to fill the defect. A 'critical-sized' defect is a bone defect which is not expected to heal in the absence of surgical intervention. It is been defined as a length equating to ≥ 50% of the cortical diameter of the bone with a minimum length of 1 cm [66]. However, it had also been defined as a length of 2–2.5 times the diameter of the bone [67].

Various options for the management of bone defects exist. For single stage procedures with < 1 cm bone defects, antibiotic-impregnated bone graft substitutes have been used with a 95.7% success rate [68]. Single stage techniques for larger bone defects include acute shortening at the fracture site with distraction osteogenesis at a distant metaphyseal site for re-lengthening using an external fixator, the placement of cancellous bone grafts, the use of vascularised bone grafts or bone transport. Two stage methods include the induced membrane (Masquelet) technique [69] and bone transport using an antibiotic-impregnated cement spacer for the first stage.

Each technique has its merits, and in a recent meta-analysis none has been shown to be superior [70]. Factors affecting decision making should include the size and location of defect, surgical experience and patient preference.

The use of antibiotic-coated intramedullary nails has been advocated in cases where infection has spread through the medullary canal as they allow for thorough debridement through reaming, dead space management whilst also providing osseous stability [71]. Following early diagnosis of FRI in cases with intramedullary devices, they can be employed to address the difficulties which would otherwise be encountered with a DAIR approach.

Local and systemic antibiotics

An important adjunct in the eradication of sepsis at the fracture site is the delivery of antibiotic therapy. Broad spectrum, empirical, intravenous antibiotic therapy should be commenced once deep samples have been obtained, and then

tailored once organisms and sensitivities are known. In the case of DAIR for acute FRI, antibiotics should continue until fracture union. For chronic infection, the optimum timescale is unknown, however, 6–12 weeks have been recommended recently, depending on the FRI characteristics [72]. The OVIVA trial (2019) showed that oral antibiotics were non-inferior to intravenous for the treatment of orthopaedic infections, and so oral antibiotics should be the preferred option post-surgery [73].

In addition to systemic therapy, the administration of local antimicrobials has been suggested to be beneficial [1]. The dead space created following debridement is an ideal environment for bacterial proliferation and biofilm creation as it is a poorly perfused environment with low oxygen and pH. Dead space management is commonly addressed by employing bone substitutes, polymethylmethacrylate (PMMA), bone grafts and biodegradable ceramics. The addition of local antibiotics in these materials offers the prospect of improved therapeutic efficacy as the agent can be delivered in higher concentrations than with systemic administration whilst also reducing the risk of the associated toxic systemic effects. Local administration further addresses the often impaired delivery in poorly perfused compromised tissues. It is important to utilise antibiotics with broad spectrum coverage. Furthermore, the effect of antibiotic addition to the mechanical properties of the construct as well as the effects of high concentrations over prolonged time intervals on fracture healing should be considered. Although generally considered safe the potential for systemic toxicity should not be neglected.

Despite the promising results that have been reported over the years, the evidence is currently lacking as to the optimal carrier, antibiotic and preferred dosing when employing local antibiotics in the management of FRI [47].

Single stage versus two stage

Single stage treatments for infected non-unions have been shown to be effective [70]. Bose et al. [74] reported 88% of patients had a united, non-infected fracture after single stage treatments varying from distraction osteogenesis to vascularised bone grafting. Single stage treatment can be used if an aseptic environment can be created, bone defects filled, skeletal stabilisation assured, and definitive soft tissue coverage provided at the same sitting.

The role of amputation

One must not forget that the aim of treatment when dealing with FRI is to give the patient a non-infected, functional limb. This can certainly be achieved using the limb salvage techniques described above. However, amputation can often provide an excellent outcome in the right patient with suitable pathology and avoid the potentially multiple procedures and complications associated with limb salvage. Barla et al. (2017) compared 20 patients with lower limb trauma who had early amputation with 16 patients who underwent limb salvage at 1-year. The amputees had shorter lengths of stay and fewer post-operative complications, but there was no difference in quality of life scores [75]. There is a paucity of data regarding outcomes of amputation for FRI but it is a treatment option that should be considered, especially in the tibia, where prosthetic options are plentiful.

Discussion

Despite the recent interest and improvements in our understanding of fracture- related infection, there are still many aspects of prevention, diagnosis and management with limited evidence available to establish the optimal strategies required.

Patient morbidity and mortality, as well as the healthcare-related costs involved, dictate the need for introducing effective preventive strategies. Optimal guidelines for prompt and cost-effective diagnostic approaches are being introduced. A multi-disciplinary approach is required at every stage.

The treating team and the patient should always be aware of the complexity of managing FRI due to the combination of difficult underlying pathology, hosts that are often compromised both locally and systemically and often the need for undertaking extensive and highly skilled surgical procedures. All treatment options must be considered including lifelong suppression, curative surgery and amputation. Patients must have ample time, information and psychosocial support to allow shared decision making before embarking on any treatment option.

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Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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