BRITISH JOURNAL OF HOSPITAL MEDICINE

Fracture-related infections

Samar A Hussain[1]
Samuel Walters[2]
Aashish K Ahluwalia[3]
Alex Trompeter[2]

Author details can be found at the end of this article

Correspondence to:
Aashish K Ahluwalia;
Aashish.ahluwalia2@nhs.net

Abstract

Fracture-related infection is a serious complication which can occur following musculoskeletal injury and is associated with significant morbidity. These complications can be challenging to recognise, and experts have provided a clearer definition of fracture-related infection to help with the diagnosis and detection of these infections. This system includes clinical, radiological and laboratory-based diagnostic features which are either confirmatory or suggestive of fracture-related infection. Treatment requires a multifaceted approach with multidisciplinary involvement, and generally a combination of surgical techniques and prolonged antibiotics, the timing and choice of which should be optimised. This article provides an evidence-based review of the British Orthopaedic Association Standards for Trauma for the diagnosis and management of fracture-related infections.

Key words: BOAST guideline; Fracture-related infection; Infection; Microbiology; Orthopaedic surgery; Trauma

Submitted: 15 December 2022; accepted following double-blind peer review: 9 May 2023

Introduction

Fracture-related infection is a serious complication which can occur following musculoskeletal injury, typically in the context of a fracture managed with surgical fixation. These complications can be challenging to recognise. A systematic review found that only 2% of studies included a clear definition of infection following fracture surgery (Metsemakers et al, 2018a). A survey of 346 healthcare professionals found no agreement between orthopaedic surgeons, radiologists and nuclear physicians regarding the optimal diagnostic strategy for fracture-related infection (Govaert et al, 2018b). This lack of clear definition has resulted in a wide variation in recognition and management of this challenging complication.

Failure to appropriately identify and manage these patients can lead to significant morbidity and mortality (Bezstarosti et al, 2019), with a considerable cost to the healthcare service (Metsemakers et al, 2017). In 2018, the AO Foundation supported the development of a consensus paper with a proposed system to help define fracture-related infection (Metsemakers et al, 2018c), and in the UK, the British Orthopaedic Association (2019) published national guidance for the management of such patients.

This article provides evidence-based guidance to aid the clinician in the detection, diagnosis and management of fracture-related infection, and summarises current British Orthopaedic Association guidance.

Pathogenesis

Fracture-related infection can occur either following exposure of bone and associated deep tissues to the external environment, for example in an open fracture or after iatrogenic introduction of pathogens during surgical fixation (exogenous), or following systemic infection originating elsewhere in the body leading to haematogenous spread of microorganisms and deposition at the fracture site (Zimmerli and Sendi, 2017; Masters et al, 2022).

After inoculation, micro-organisms can colonise, proliferate and form a biofilm within hours, which renders them less susceptible to the effects of systemic antibiotics (Kranjec et al, 2021). Biofilms are aggregates of microorganisms enclosed in an extracellular polymeric substance matrix (Donlan, 2002) and can form on biotic (living) tissues, or abiotic surfaces such as dead bone or implants, as is often the case in fracture-related infection. There is minimal blood supply to implants used for fracture fixation surgery, which further reduces the ability to eradicate infection with systemic antibiotics alone (Masters et al, 2022).

How to cite this article:
Hussain SA, Walters S, Ahluwalia AK, Trompeter A. Fracture-related infections. Br J Hosp Med. 2023. https://doi.org/10.12968/hmed.2022.0545

Risk factors

Risk factors that contribute to the increased likelihood of developing fracture-related infection include patient-related factors such as smoking (Scolaro et al, 2014), male gender and diabetes mellitus (Kortram et al, 2017). The presence of an open fracture significantly increases the risk of deep infection (Papakostidis et al, 2011). The incidence of fracture-related infection is approximately 1–2% for closed fractures, but up to 30% for open fractures (Metsemakers et al, 2018b). In terms of surgical factors, the importance of early wound coverage in reducing the risk of infection is well recognised (British Orthopaedic Association, 2017), as well as stable fracture fixation, with unstable bone fragments more likely to sequester infection (Worlock et al, 1994).

Microbiology

Table 1 lists the most common pathogens that cause fracture-related infection (Trampuz and Zimmerli, 2006; Kuehl et al, 2019). Polymicrobial infection is not uncommon (Depypere et al, 2020b), and more so following open fractures. Knowledge of the likely causative microbes helps decision making with regards to empirical antibiotic therapy while awaiting microbiological results from samples.

Prevention

It is preferable to prevent infection from developing in the first instance. The British Orthopaedic Association (2019) guideline emphasises that measures should be implemented to prevent fracture-related infections developing, and all NHS trusts or equivalent responsible bodies should adhere to standards for preventing such infections.

Patients with open fractures should be managed according to British Orthopaedic Association Standards for Trauma (British Orthopaedic Association, 2017) and National Institute for Health and Care Excellence (2022) guidelines for open fractures. These highlight the importance of early (within 1 hour of injury) administration of intravenous antibiotics, thorough examination of the affected limb including clinical photography and appropriate surgical management of the fracture as well as soft tissue. Definitive soft tissue coverage should be achieved within 72 hours of injury, if not possible at the time of initial debridement, and internal fixation should only be considered if it can be immediately followed by definitive soft tissue cover (British Orthopaedic Association, 2017).

Patient awareness of fracture-related infection is important to encourage them to seek help appropriately. Patients should be counselled regarding the risk of wound or implant infection when undergoing orthopaedic surgery. They should be given written advice about signs and symptoms of fracture-related infection upon discharge, and primary care clinicians should have ready access to guidance on how to manage and appropriately refer patients with suspected fracture-related infection.

Diagnosis

The presentation of a patient with an infection may be varied and can pose a diagnostic challenge. Experts have provided a definition of fracture-related infection to help with

Table 1. Common pathogens involved in fracture-related infection

Microorganism	Frequency
Staphylococcus aureus	30–42%
Coagulase-negative staphylococci	20–39%
Enterobacteriaceae	14–27%
Anaerobes	16%
Streptococci	11%

From Depypere et al (2020b)

diagnosis and detection of these infections (Metsemakers et al, 2018c; McNally et al, 2020). Clinical signs and symptoms can be classified into two confirmatory and five suggestive criteria (Table 2). Superficial signs can range from relatively mild erythema to pronounced wound breakdown or sinus formation (Figure 1). Following surgical management and sampling, three (previously two) further confirmatory criteria and one suggestive criterion can be fulfilled based on the results of the laboratory investigations (Table 3). If confirmatory criteria are present (eg sinus, fistula, wound breakdown or pus), the diagnosis is not in doubt, but the presence of suggestive criteria is not necessarily diagnostic of fracture-related infection and may represent an alternative pathology, so should prompt further investigation.

Investigations of patients with suspected fracture-related infection should be aligned to these diagnostic criteria. All febrile or systemically unwell patients should have blood cultures taken, and all patients should have blood tests including levels of inflammatory markers. Serial clinical examinations and photography of the wound is useful as it allows more accurate monitoring of clinical progression.

Patients suspected of having fracture-related infection should have plain X-rays taken to assess for implant loosening, periosteal reaction, bone lysis, failure of progression of bone healing or sequestrum (dead bone) formation (Figure 2) (Li et al, 2021). Computed tomography and magnetic resonance imaging can be useful adjuncts. Computed tomography provides better information about fracture union and the extent of bone necrosis, and magnetic resonance imaging can indicate the extent of soft tissue involvement (Trampuz and Zimmerli, 2006), but their utility may be limited by artefact from implants. 18F-fluorodeoxyglucose

Table 2. Criteria for diagnosis of a fracture-related infection before surgical management or sampling

Confirmatory criteria	Fistula, sinus or wound breakdown (with communication to the bone or the implant)
	Purulent drainage from the wound or presence of pus during surgery
Suggestive criteria	Clinical signs – any one of: ■ Pain (without weight-bearing, increasing over time, new-onset) ■ Local redness ■ Local swelling ■ Increased local temperature ■ Fever (single oral temperature measurement of ≥38.3°C)
	Radiological signs – any one of: ■ Bone lysis (at the fracture site, around the implant) ■ Implant loosening ■ Sequestration (occurring over time) ■ Failure of progression of bone healing (ie non-union) ■ Presence of periosteal bone formation (eg at localisations other than the fracture site or in case of a consolidated fracture)
	Elevated serum levels of inflammatory markers: in patients with musculoskeletal trauma, these should be interpreted with caution. They are included as suggestive signs in case of a secondary rise (after an initial decrease) or a consistent elevation over a period of time, and after exclusion of other infectious foci or inflammatory processes: ■ Erythrocyte sedimentation rate ■ White blood cell count ■ C-reactive protein
	Persistent, increasing or new onset wound drainage, beyond the first few days postoperatively, without solid alternative explanation
	New onset of joint effusion in fracture patients. Fracture-related infection can present as an adjacent septic arthritis in the following cases: ■ Implant material which penetrates the joint capsule (eg femoral nailing) ■ Intra-articular fractures

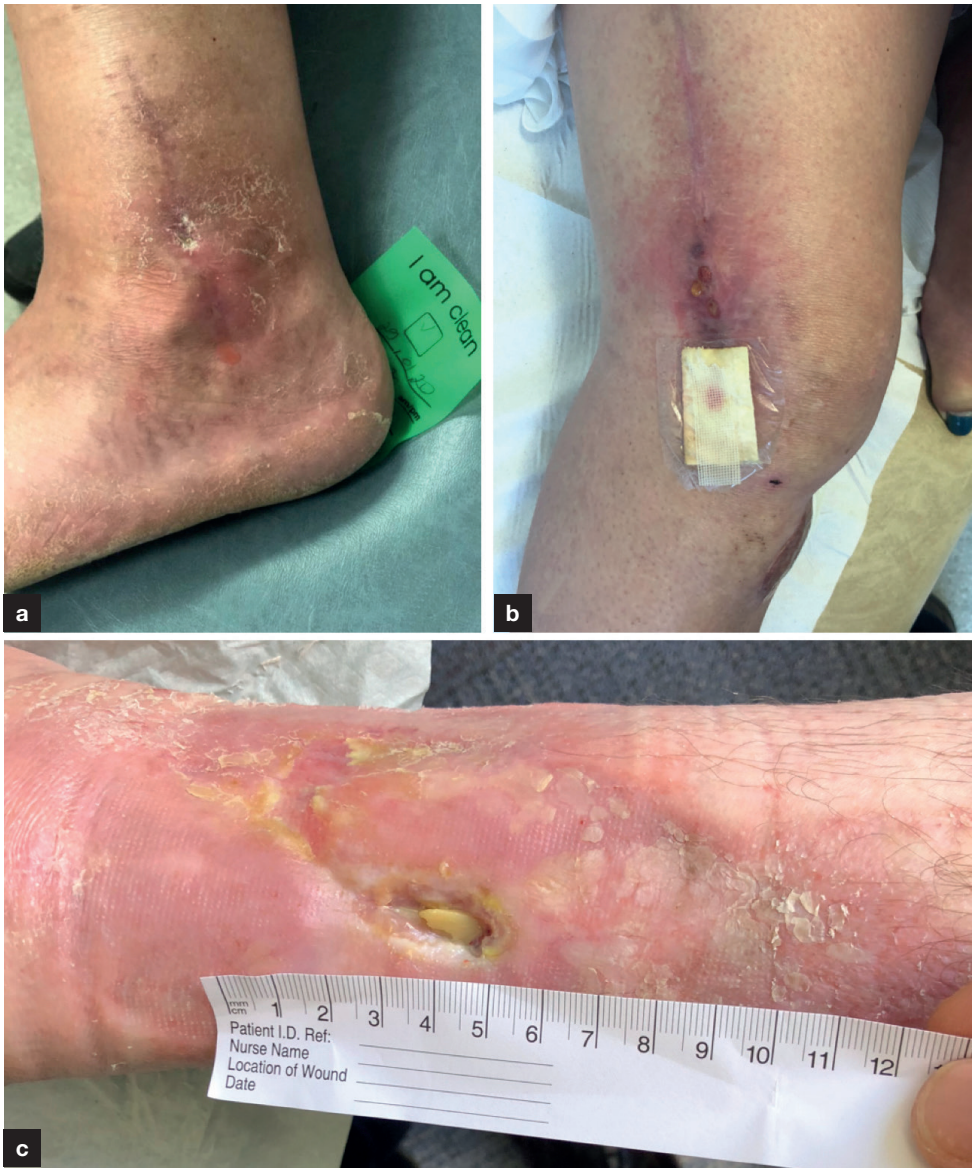

Figure 1. Wounds with signs of infection following open reduction internal fixation. a. Mild erythema and swelling. b. Erythema, multiple sinus formation and discharge. c. Pronounced erythema, sinus formation and wound breakdown.

Table 3. Criteria for diagnosis of a fracture-related infection after surgical management or sampling

In case of tissue samples, multiple specimens (ideally five for culture and two for histopathology) 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	
Confirmatory criteria	Phenotypically indistinguishable pathogens identified by culture from at least two separate deep tissue or implant (including sonication fluid) specimens taken during surgery
	Presence of microorganism in deep tissue taken during surgery, as confirmed by histopathological examination using specific staining techniques for bacteria or fungi
	More than five polymorphonuclear neutrophils per high-power field on histopathological examination
Suggestive criteria	A pathogenic organism identified by culture from a single deep tissue or implant (including sonication fluid) specimen taken during surgery

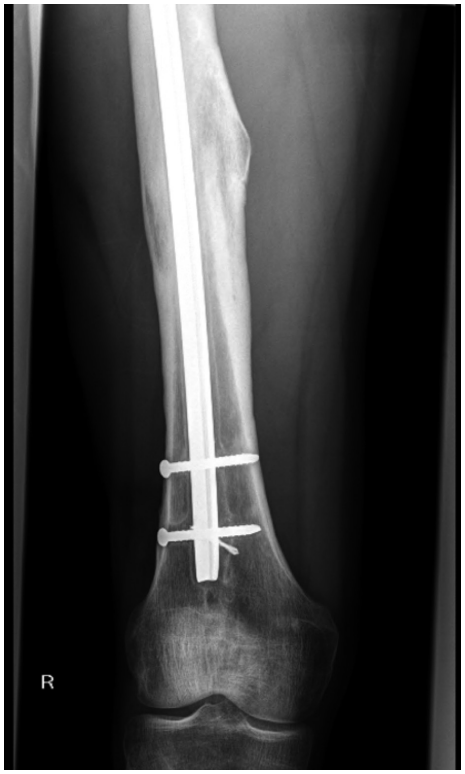

Figure 2. X-ray demonstrating implant loosening and bone lysis surrounding an implant (femoral intramedullary nail). The broken drill bit (at the level of the distal screw) may be a sign of 'surgical difficulty' which may be associated with increased risk of infection.

positron emission tomography has a diagnostic accuracy of 0.83 and a negative predictive value of 0.91 (Lemans et al, 2019), with the most reliable results seen when the scan is performed at least 1 month after surgery. White blood cell scintigraphy has a diagnostic accuracy of 0.92 with a negative predictive value of 0.93, and its accuracy is not influenced by recent surgery (Govaert et al, 2018a), but it is logistically challenging (requires two scans at different time points), and is less accurate for diagnosing infections of the axial skeleton.

Early sampling should be performed – this is typically at surgical debridement in order to obtain deep tissue samples, but in certain circumstances may be done under radiological guidance (eg aspiration of a collection). Patients that undergo debridement surgery should have five separate deep tissue samples taken from different sites around the fracture, ideally from the implant–bone interface, using a 'no-touch technique' and separate sterile instruments for each sample, and sent for microscopy and culture. Chronic infections (arbitrarily defined as longer than 6 weeks) can commonly be caused by commensal organisms, so sampling must be meticulous to avoid false positives or negatives (Govaert et al, 2020). It is also recommended that patients with chronic infections, or acute cases in which the diagnosis is in doubt, should have two additional samples sent for histopathological examination to look for the presence of microorganisms or polymorphonuclear neutrophils (British Orthopaedic Association, 2019). Following further expert review, the presence of more than five polymorphonuclear neutrophils within one high-power field on histopathological examination was added as the fifth confirmatory diagnostic criteria (Morgenstern et al, 2018). These sampling principles should also be followed in elective procedures to revise metalwork (eg for non-union), even if there is low clinical suspicion of infection.

Sonication uses low frequency ultrasound to dislodge pathogens from the surface of implants into a fluid, which can be cultured. This is a useful tool in cases of prosthetic joint infection, but its utility in fracture-related infection remains unclear (Sebastian et al, 2018; Govaert et al, 2020). It has been suggested that it could be useful in patients that have received antibiotic treatment before sampling (Depypere et al, 2020b; Stephan et al, 2021).

Further work is necessary to develop tools to diagnose and treat fracture-related infection. As an example, the use of molecular diagnostics such as 16S ribosomal RNA polymerase

chain reaction may provide an alternative to tissue culture for pathogen identification. Molecular diagnostics are expected to deliver greater diagnostic accuracy and speed (Renz et al, 2018), but tissue culture is a more accessible method of detecting implant-related infection. Additionally, polymerase chain reaction cannot provide any information about antibiotic susceptibility of the microorganism. The technique used to provide samples for polymerase chain reaction can affect reliability, with deep tissue samples or sonication fluid being more reliable than swabs (Govaert et al, 2020).

Management

As with any infective process, the first priority is ensuring that the patient is not systemically compromised. A thorough medical assessment should be conducted, ensuring cardiovascular and respiratory stability. Routine blood tests including inflammatory markers should be taken, and ideally blood cultures taken before starting antibiotics. However, in an unstable septic patient, antibiotics should not be delayed.

Many patients with fracture-related infection are systemically stable, and antibiotic treatment should be withheld until after sampling, as this may improve the chances of accurate microbiological diagnosis. Similarly, if antibiotics have already been started in a stable patient, they should be stopped (Depypere et al, 2020b; Govaert et al, 2020). Early consultation with a microbiologist should be sought to determine an optimum antibiotic-free period before tissue samples are taken. Patients with chronic infections should not receive antibiotics for a minimum of 2 weeks before samples are collected.

The patient should be reviewed in an appropriate clinic by a consultant within 48 hours. If fracture-related infection is deemed likely, the patient should be managed by a multidisciplinary team, which may consist of orthopaedic surgeons, plastic surgeons, microbiologists, radiologists and therapists, and this may also involve referral to a tertiary centre depending on local policy.

Once the patient has been reviewed by an appropriate service, if fracture-related infection is still suspected, surgical management is generally required (see below). Once samples have been taken, broad-spectrum empirical antibiotics may be started. The antibiotic(s) of choice may vary according to local practice and trusts should have published policies. Antibiotics should be reviewed after 48 hours, when preliminary culture results should be available. At this point, further discussion with microbiology specialists is useful to ensure treatment is narrowed and culture specific. The microbiology team should also be able to provide advice regarding duration of treatment.

In cases where new implants are to be inserted at the time of surgery (eg exchange of metalwork), it may be preferable to give antibiotics slightly earlier. There is limited evidence in relation to fracture-related infection, but a study of patients with prosthetic joint infection undergoing revision surgery compared administration of antibiotics at induction of anaesthesia with administration after sampling, and showed no significant differences in microorganisms isolated, and a trend towards lower re-infection rates of the new prosthesis when antibiotics were given at induction (Wouthuyzen-Bakker et al, 2017).

A multidisciplinary team is invaluable in making decisions for complex cases including patients with late or recurrent infections, those that do not respond to initial treatment, or those with infected non-unions, or major soft tissue and bone defects.

Surgical management

Surgical intervention plays a key role in the management of fracture-related infection. The first principles of surgical management are to collect deep samples as previously described, and systematically debride any devitalised or non-viable tissues. This may involve draining any collections or removing sequestra.

Debridement may leave a bone or soft tissue defect, creating dead space, which is an area of relatively poor perfusion and an ideal environment for bacterial proliferation and potential reinfection. Dead space can be managed by filling the defect with substances such as bone graft or antibiotic-impregnated spacers or beads made from bone cement or bioabsorbable substances such as calcium sulphate, or by acutely shortening the limb (Zimmerli and Sendi, 2017; Metsemakers et al, 2020).

Unlike in cases of prosthetic joint infection, metalwork used in fracture fixation can be removed once bone fragments have united, but this healing process is often slower or insufficient in the presence of infection, presenting further challenges. Debridement, antimicrobial therapy and implant retention can be an effective strategy in early fracture-related infection (within 6 weeks of index procedure), providing that the implant remains well fixed and the fracture stable (Hoit et al, 2020). This strategy achieved successful bony union in 71% of patients (Berkes et al, 2010). Once fracture union has occurred, which may be confirmed on imaging such as computed tomography, the infected prosthesis may be removed (Depypere et al, 2020a).

In later presentations, or when stability is lost, the implants may need to be removed and the fracture stabilised by another means. Chronic infections may be more difficult to manage and often result in non-union. In these cases, surgical management is frequently prolonged and complex reconstruction may be required (Bezstarosti et al, 2019). In addition to fracture stability, soft tissue coverage must be considered to provide a suitable environment for fracture healing. This can be challenging when faced with significant soft tissue defects, and early input from the plastic surgery team is vital in these cases to plan and achieve closure or reconstruction as required.

A novel technique of interest is the local administration of bacteriophages (viruses that selectively infect and lyse bacteria). Although they were developed as a treatment for bacterial infection in the early 20th century, the advent of antibiotics saw a decline in the popularity of bacteriophages, thus there are few modern studies evaluating their utility. However, in an era of growing concerns about antibiotic resistance, they may prove a useful adjunct in treating infections (Yilmaz et al, 2013; Onsea et al, 2021).

Infections in a limb that do not resolve, despite prolonged medical and surgical therapy aiming to salvage the limb, may be best treated with amputation. This decision should be made in conjunction with the patient, considering individual functional requirements and patient factors. Care should be taken to fully remove infected tissue during amputation, as residual infection following amputation is a serious cause of morbidity and mortality (Jain et al, 2013).

Conclusions

Although relatively rare, fracture-related infection causes significant morbidity in affected patients. An awareness of the clinical signs and symptoms combined with thorough investigation is needed to diagnose and appropriately treat infection. Antibiotic therapy alone may not be sufficient, and often better outcomes can be achieved by more aggressive early intervention. It is essential that patients have a multifaceted approach to treatment, with multidisciplinary involvement.

Key points

- Fracture-related infection is a serious complication, associated with significant morbidity, which can occur following musculoskeletal injury.
- Recent guidelines provide greater clarity with clinical, radiological and laboratory-based features to diagnose fracture-related infection, and principles for treatment.
- Radiological investigations that may be useful include plain X-rays, computed tomography and magnetic resonance imaging, as well as nuclear medicine imaging modalities.
- Laboratory-based investigations include microscopy and culture, and histopathological examination, and there is a developing role for molecular diagnostic procedures.
- Treatment of fracture-related infection requires a multifaceted approach with multidisciplinary involvement, and generally a combination of surgical techniques and prolonged antibiotics, with microbiology specialist input.
- Surgical treatment consists of deep sampling, debridement of devitalised tissue, dead space management, fracture stabilisation and soft tissue coverage.

Curriculum checklist

This article addresses the following requirements from the trauma and orthopaedic surgery training curriculum:

- Manages an outpatient clinic
- Professional knowledge: applied clinical (basic) science – pathology
- Professional knowledge: trauma – complications.

Clear diagnostic criteria and guidelines for the management of fracture-related infection have been developed. This has been an important step forward, but further work is still needed to optimise diagnostic methods and develop novel techniques for detecting and treating such infections.

Author details

[1]Major Trauma Department, St Mary's Hospital, London, UK

[2]Orthopaedic Trauma/Limb Reconstruction Unit, St George's University Hospital, London, UK

[3]Department of Trauma and Orthopaedic Surgery, University College Hospital, London, UK

Conflicts of interest

A Trompeter is a member of the British Orthopaedic Association Trauma Committee, who are responsible for producing the British Orthopaedic Association Standards for Trauma guidelines. SA Hussain, S Walters and A Ahluwalia declare that they have no conflicts of interest.

Acknowledgements

All figures provided by A Trompeter with patient permission.

References

Berkes M, Obremskey WT, Scannell B et al. Maintenance of hardware after early postoperative infection following fracture internal fixation. J Bone Joint Surg Am. 2010;92(4):823–828. https://doi.org/10.2106/JBJS.I.00470

Bezstarosti H, Van Lieshout EMM, Voskamp LW et al. Insights into treatment and outcome of fracture-related infection: a systematic literature review. Arch Orthop Trauma Surg. 2019;139(1):61–72. https://doi.org/10.1007/s00402-018-3048-0

British Orthopaedic Association. BOAST – open fractures. 2017. https://www.boa.ac.uk/resources/boast-4-pdf.html (accessed 29 June 2023)

British Orthopaedic Association. BOAST – fracture related infections (FRI). 2019. https://www.boa.ac.uk/resources/boast-fracture-related-infections.html (accessed 29 June 2023)

Depypere M, Kuehl R, Metsemakers W-J et al. Recommendations for systemic antimicrobial therapy in fracture-related infection: a consensus from an international expert group. J Orthop Trauma. 2020a;34(1):30–41. https://doi.org/10.1097/BOT.0000000000001626

Depypere M, Morgenstern M, Kuehl R et al. Pathogenesis and management of fracture-related infection. Clin Microbiol Infect. 2020b;26(5):572–578. https://doi.org/10.1016/j.cmi.2019.08.006

Donlan RM. Biofilms: microbial life on surfaces. Emerg Infect Dis. 2002;8(9):881–890. https://doi.org/10.3201/eid0809.020063

Govaert GAM, Bosch P, IJpma FFA et al. High diagnostic accuracy of white blood cell scintigraphy for fracture related infections: results of a large retrospective single-center study. Injury. 2018a;49(6):1085–1090. https://doi.org/10.1016/j.injury.2018.03.018

Govaert GAM, Glaudemans AWJM, Ploegmakers JJW et al. Diagnostic strategies for posttraumatic osteomyelitis: a survey amongst Dutch medical specialists demonstrates the need for a consensus protocol. Eur J Trauma Emerg Surg. 2018b;44(3):417–426. https://doi.org/10.1007/s00068-017-0783-9

Govaert GAM, Kuehl R, Atkins BL et al. Diagnosing fracture-related infection: current concepts and recommendations. J Orthop Trauma. 2020;34(1):8–17. https://doi.org/10.1097/BOT.0000000000001614

Hoit G, Bonyun M, Nauth A. Hardware considerations in infection and nonunion management: when and how to revise the fixation. OTA Int. 2020;3(1):e055. https://doi.org/10.1097/OI9.0000000000000055

Jain A, Glass GE, Ahmadi H et al. Delayed amputation following trauma increases residual lower limb infection. J Plast Reconstr Aesthet Surg. 2013;66(4):531–537. https://doi.org/10.1016/j.bjps.2012.11.026

Kortram K, Bezstarosti H, Metsemakers W-J et al. Risk factors for infectious complications after open fractures; a systematic review and meta-analysis. Int Orthop. 2017;41(10):1965–1982. https://doi.org/10.1007/s00264-017-3556-5

Kranjec C, Morales Angeles D, Torrissen Mårli M et al. Staphylococcal biofilms: challenges and novel therapeutic perspectives. Antibiotics (Basel). 2021;10(2):131. https://doi.org/10.3390/antibiotics10020131

Kuehl R, Tschudin-Sutter S, Morgenstern M et al. Time-dependent differences in management and microbiology of orthopaedic internal fixation-associated infections: an observational prospective study with 229 patients. Clin Microbiol Infect. 2019;25(1):76–81. https://doi.org/10.1016/j.cmi.2018.03.040

Lemans JVC, Hobbelink MGG, IJpma FFA et al. The diagnostic accuracy of 18F-FDG PET/CT in diagnosing fracture-related infections. Eur J Nucl Med Mol Imaging. 2019;46(4):999–1008. https://doi.org/10.1007/s00259-018-4218-6

Li C, Renz N, Trampuz A, Ojeda-Thies C. The value of conventional radiographs for diagnosing internal fixation-associated infection. BMC Musculoskelet Disord. 2021;22(1):411. https://doi.org/10.1186/s12891-021-04170-3

Masters EA, Ricciardi BF, Bentley KLDM et al. Skeletal infections: microbial pathogenesis, immunity and clinical management. Nat Rev Microbiol. 2022;20(7):385–400. https://doi.org/10.1038/s41579-022-00686-0

McNally M, Govaert G, Dudareva M, Morgenstern M, Metsemakers W-J. Definition and diagnosis of fracture-related infection. EFORT Open Rev. 2020;5(10):614–619. https://doi.org/10.1302/2058-5241.5.190072

Metsemakers W-J, Smeets B, Nijs S, Hoekstra H. Infection after fracture fixation of the tibia: analysis of healthcare utilization and related costs. Injury. 2017;48(6):1204–1210. https://doi.org/10.1016/j.injury.2017.03.030

Metsemakers WJ, Kortram K, Morgenstern M et al. Definition of infection after fracture fixation: a systematic review of randomized controlled trials to evaluate current practice. Injury. 2018a;49(3):497–504. https://doi.org/10.1016/j.injury.2017.02.010

Metsemakers WJ, Kuehl R, Moriarty TF et al. Infection after fracture fixation: current surgical and microbiological concepts. Injury. 2018b;49(3):511–522. https://doi.org/10.1016/j.injury.2016.09.019

Metsemakers WJ, Morgenstern M, McNally MA et al. Fracture-related infection: a consensus on definition from an international expert group. Injury. 2018c;49(3):505–510. https://doi.org/10.1016/j.injury.2017.08.040

Metsemakers W-J, Fragomen AT, Moriarty TF et al. Evidence-based recommendations for local antimicrobial strategies and dead space management in fracture-related infection. J Orthop Trauma. 2020;34(1):18–29. https://doi.org/10.1097/BOT.0000000000001615

Morgenstern M, Athanasou NA, Ferguson JY et al. The value of quantitative histology in the diagnosis of fracture-related infection. Bone Joint J. 2018;100-B(7):966–972. https://doi.org/10.1302/0301-620X.100B7.BJJ-2018-0052.R1

National Institute for Health and Care Excellence. Fractures (complex): assessment and management. 2022. https://www.nice.org.uk/guidance/ng37/chapter/Recommendations#hospital-settings (accessed 29 June 2023)

Onsea J, Post V, Buchholz T et al. Bacteriophage therapy for the prevention and treatment of fracture-related infection caused by Staphylococcus aureus: a preclinical study. Microbiol Spectr. 2021;9(3):e01736-21. https://doi.org/10.1128/spectrum.01736-21

Papakostidis C, Kanakaris NK, Pretel J et al. Prevalence of complications of open tibial shaft fractures stratified as per the Gustilo-Anderson classification. Injury. 2011;42(12):1408–1415. https://doi.org/10.1016/j.injury.2011.10.015

Renz N, Cabric S, Morgenstern C, Schuetz MA, Trampuz A. Value of PCR in sonication fluid for the diagnosis of orthopedic hardware-associated infections: has the molecular era arrived? Injury. 2018;49(4):806–811. https://doi.org/10.1016/j.injury.2018.02.018

Scolaro JA, Schenker ML, Yannascoli S et al. Cigarette smoking increases complications following fracture: a systematic review. J Bone Joint Surg Am. 2014;96(8):674–681. https://doi.org/10.2106/JBJS.M.00081

Sebastian S, Malhotra R, Sreenivas V et al. Sonication of orthopaedic implants: a valuable technique for diagnosis of prosthetic joint infections. J Microbiol Methods. 2018;146:51–54. https://doi.org/10.1016/j.mimet.2018.01.015

Stephan A, Thürmer A, Glauche I et al. Does preoperative antibiotic prophylaxis affect sonication-based diagnosis in implant-associated infection? J Orthop Res. 2021;39(12):2646–2652. https://doi.org/10.1002/jor.25015

Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. Injury. 2006;37(2):S59–S66. https://doi.org/10.1016/j.injury.2006.04.010

Worlock P, Slack R, Harvey L, Mawhinney R. The prevention of infection in open fractures: an experimental study of the effect of fracture stability. Injury. 1994;25(1):31–38. https://doi.org/10.1016/0020-1383(94)90181-3

Wouthuyzen-Bakker M, Tornero E, Claret G et al. Withholding preoperative antibiotic prophylaxis in knee prosthesis revision: a retrospective analysis on culture results and risk of infection. J Arthroplasty. 2017;32(9):2829–2833. https://doi.org/10.1016/j.arth.2017.03.064

Yilmaz C, Colak M, Yilmaz BC et al. Bacteriophage therapy in implant-related infections: an experimental study. J Bone Joint Surg Am. 2013;95(2):117–125. https://doi.org/10.2106/JBJS.K.01135

Zimmerli W, Sendi P. Orthopaedic biofilm infections. APMIS. 2017;125(4):353–364. https://doi.org/10.1111/apm.12687