Injury, Int. J. Care Injured 50 (2019) 1952–1958

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Chinese expert consensus on diagnosis and treatment of infection after fracture fixation☆

Nan Jiang[a,1], Bo-wei Wang[a,1], Yi-min Chai[b], Xin-bao Wu[c,*], Pei-fu Tang[d,*], Ying-ze Zhang[e,*], Bin Yu[a,*]

[a] Department of Orthopaedics & Traumatology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China
[b] Department of Orthopaedics, The Sixth People's Hospital of Shanghai Jiao Tong University, Shanghai, PR China
[c] Department of Orthopaedics & Traumatology, Beijing Jishuitan Hospital, Beijing, PR China
[d] Department of Orthopaedics, Chinese PLA General Hospital, Beijing, PR China
[e] Department of Orthopaedics, The Third Hospital of Hebei Medical University, Shijiazhuang, PR China

ARTICLE INFO

Keywords:
Fracture-related infections
Chronic osteomyelitis
Diagnosis
Treatment
Chinese expert consensus

ABSTRACT

Currently, accurate diagnosis and successful treatment of infection after fracture fixation (IAFF) still impose great challenges. According to the onset of infection symptoms after implantation, IAFF is classified as early infection (<2 weeks), delayed infection (2∼10 weeks) and late infection (>10 weeks). Confirmation of IAFF should be supported by histopathological tests of intraoperative specimens which confirm infection, cultures from at least two suspected infection sites which reveal the same pathogen, a definite sinus or fistula which connects directly the bone or the implant, and purulent drainage from the wound or presence of pus during surgery. Diagnosis of IAFF is built on comprehensive assessment of medical history, clinical signs and symptoms of the patient, and imaging and laboratory tests. The gold standard of diagnosis is histopathological tests. Treatment of IAFF consists of radical debridement, adequate irrigation, implant handling, systematic and local antibiotics, reconstruction of osseous and/or soft tissue defects, and functional rehabilitation of an affected limb. Early accurate diagnosis and appropriate treatment of IAFF play a key role in increasing the cure rate, reducing infection recurrence and disability risk, restoring limb function and improving quality of life of the patient.

Introduction

Currently, infection after fracture fixation (IAFF) remains one of the most challenging disorders for orthopaedists, as it is sometimes difficult to diagnose and intractable to cure. Ineffective control of IAFF may eventually lead to occurrence of chronic osteomyelitis, a long-term disorder with persistent bone infection and a high risk of recurrence and disability. Additionally, IAFF also exerts a social-economic burden on the patients and their families. Early accurate diagnosis and appropriate treatment of IAFF are essential for a high cure rate, decrease risk of recurrence and disability, limb functional restoration and decent quality of life of the patient.

Definition

Recent studies demonstrate that there has been no consensus regarding IAFF definition. Most of the previous investigations did not provide a detailed definition of IAFF but used different parameters to describe the disorder, such as positive cultures, purulent discharge or drainage and elevation of C-reactive protein (CRP) [1,2]. Although both IAFF and periprosthetic joint infection (PJI) belong to implant associated infection, they differ in diagnosis, treatment and prognosis. IAFF should be regarded as a special type of disorder different from PJI [2].

It is recommended that IAFF should be defined as infection of the osseous tissue contacting the implant with or without infection of the surrounding soft tissue following implantation of the fracture device, resulting from contamination of pathogens and/or compromised immunity of the host.

☆ This article was originally published in Chinese in the Chinese Journal of Orthopaedic Trauma in November, 2018 (Volume 20, issue 11, pages 929–936). The English translation is printed here with the kind permission of the Chinese Journal of Orthopaedic Trauma.

* Corresponding authors.
E-mail addresses: wuxinbao@jsthospital.org (X.-b. Wu), pftang301@126.com (P.-f. Tang), yzling_liu@163.com (Y.-z. Zhang), yubin@smu.edu.cn (B. Yu).

[1] These authors have contributed equally to this work.

https://doi.org/10.1016/j.injury.2019.08.002
0020-1383/

Classification

Time classification

According to the onset of its symptoms after implantation of fracture devices, IAFF can be classified into three stages [3]: early infection (<2 weeks), delayed infection (2∼10 weeks) and late infection (>10 weeks). Early infection is frequently caused by highly virulent pathogens, such as *Staphylococcus aureus* [4]. Although the causative bacteria may have already formed a biofilm, they may remain in an "immature" phase. Inflammation-associated changes in bone and soft tissues are not obvious. Delayed infection is usually caused by less virulent pathogens, such as *Staphylococcus epidermidis* [4]. Owing to persistent infection, the biofilm matures and becomes more resistant to antibiotics and host defenses. In this stage, infected osseous tissue reveals signs of osteolysis and nonunion while surrounding infected soft tissue shows signs of further necrosis [3]. Low-virulence microorganisms are the primary causative agents for late infection. Long-term infection results in compromised fracture healing and chronic osteomyelitis, characterized by inflammation-associated osteolysis with new bone formation [5]. Different infection durations result in different histopathological changes in bone and soft tissues which determine varied treatment strategies.

Cierny-mader classification for osteomyelitis [6]

Cierny-Mader classification involves anatomy and host physiology. Its anatomic classification consists of four types. Type I is medullary infection, type II superficial infection, type III localized infection and type IV diffuse osteomyelitis. The host physical status is divided into three classes. Host A shows a good immune system and delivery, host B is compromised locally (B^L) or systemically (B^S) or both (B^{LS}), and host C is not a surgical candidate due to its poor systemic condition and prognosis. Selection of a treatment strategy should be built on both the anatomy type and host physiologic class.

Epidemiology

Incidence

It depends on the interactions between environmental factors and host factors whether infection may develop after implantation of a fracture device. Environmental factors include injury feature, fracture location and type, soft tissue injury, pathogen type, treatment time and strategy. Host factors refer to immune and nutritional status, and systematic and local underlying diseases [7]. According to a recent study [8], incidence of IAFF ranged from 0.4% to 16.1%, with an average of 5%. The incidence of IAFF was approximate 1% after a closed fracture, and 15% [9] or over 30% [4] or even up to 55% [10] after an open fracture. It differed with different fractured sites, ranging from 2.1% to 11.1% after surgery of proximal tibia (with an average of 6.9% [11–13]) and from 1.1% to 6.1% after ankle fracture surgery (with an average of 4.1% [14,15]). In addition, it might have been influenced by geographical location and climate [16].

Risk factors and comorbidities

Smoking is one of the most important and independent risk factors of IAFF [10,17] and its recurrence. Therefore, smokers should be well informed and smoking cessation is recommended before IAFF therapy. Other systematic risk factors include diabetes mellitus (including preoperative hyperglycemia), obesity, malnutrition, alcohol abuse, compromised immunity or immunodeficiency, anemia, allergies against implants, advanced age, chronic hypoxia, malignant diseases, hepatic or renal failure et al. [10,18] Local factors are hypoperfusion of the traumatized region, venous stasis, chronic lymphedema, radiogenic fibrosis and severe scarring owing to preceding surgery et al [10,18].

Several recent studies indicated that patients with chronic osteomyelitis experienced significantly increased risks of other system diseases, such as intracerebral hemorrhage [19], acute pancreatitis [20], coronary heart disease [21], diabetes mellitus [22] and even depression [23].

Healthcare cost

A recent survey [24] revealed that total healthcare costs for patients with tibia infection were approximately 6.5-times higher compared to the uninfected patients, averaging 44,468 Euros. Additionally, the median lengths of antibiotic therapy and hospital stay for infected patients were, respectively, 11-fold and 7.7-fold longer than those for non-infected ones. According to the data of 278 in-patients with post-traumatic osteomyelitis at the Department of Orthopaedics & Traumatology, Nanfang Hospital, Southern Medical University over a period of 3 years, the direct healthcare cost for infected patients was 4.8 times higher than that for non-infected ones, totaling about 73,500 RMB yuan (about 10,500 US dollars) for each [25].

Diagnosis

Diagnosis of IAFF should be made according to medical history, clinical signs and symptoms of the patient, imaging data including X-ray, ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and nuclear medical examinations, laboratory tests of serological levels of inflammatory biomarkers, pathogen culture and identification, and a histopathological test. It is recommended that the histopathological test should be the gold standard for diagnosis of IAFF.

Confirmatory criteria of IAFF

In the year 2017, with the support of the AO Foundation, an international expert group defined four confirmatory criteria for IAFF [26]: fistula, sinus or wound breakdown with communication to the bone or the implant; purulent drainage from the wound or presence of pus during surgery; phenotypically indistinguishable pathogens identified by culture from at least two separate deep tissue/implant specimens; histopathological examination confirming presence of microorganisms in deep tissue taken during surgery.

Medical history, clinical signs and symptoms

The injury to bone and soft tissue regarding its feature, site and severity should be assessed as well as the interventions the patient has received (including antibiotics and operations) in IAFF patients who often have a definite history of injury and/or surgery. Meanwhile, attention should be paid to comorbidities of the IAFF patients, especially the high-risk factors. In an early infection stage, the patient usually presents with classic signs of acute inflammation (local redness, swelling, heat and pain), wound healing disturbance and local hematoma. In addition, systematic signs can also appear, such as fever and lethargy [26]. In a delayed infection stage, the patient can present with symptoms in the early and late infection stages, such as local hematoma (early infection) and sinus/fistula (late infection). In a late infection stage, the patient usually presents with untypical or subtle symptoms, like compromised limb function, local swelling, tenderness, erythema and sinus/fistula, mostly lacking systemic manifestations [3].

Imaging examinations

Imaging examinations include X-ray, ultrasound, CT, MRI and nuclear medical ones [9]. It is recommended that X-ray should be routine for patients suspected of IAFF [27,28] as it can preliminarily evaluate fracture reduction, bone healing and implant status. Typical X-ray image characteristics of IAFF are bone erosion and reactive new bone formation away from fracture site. In suspicion of IAFF associated with low-virulent pathogens or atypical X-ray manifestations in an early stage, continuously dynamic radiographs and close follow-ups are necessary to detect any abnormality in time. Ultrasound can assess status of soft tissue infection, such as local abscess formation. Compared with X-ray, CT scan can depict osseous changes better, such as fracture consolidation, position of fracture device and situation of bone nonunion. Additionally, CT can be used to find original position of bone lesion connecting the sinus tract. Moreover, once intramedullary gas is detected by CT scan, a reliable sign of acute infection is established. However, CT is not capable of evaluating soft tissue infection, not sensitive enough for bone marrow oedema and easily disturbed by metallic implants in image quality. MRI is valuable for diagnosis of early infection as it can detect changes of bone marrow oedema early (1∼2 days) after infection [27] and is sensitive to changes in osseous tissue and surrounding soft tissue after infection so that it can clearly show the scope of infection in bone and soft tissue. Therefore, MRI helps to determine the area of debridement. However, MRI is also prone to disturbance from metallic implants.

Nuclear medical examinations mainly include three-phase bone scintigraphy, leukocyte scan and positron emission tomography (PET). Bone scintigraphy can detect whether multiple infection lesions exist throughout the body. However, its value is limited in distinguishing infection in the patients who suffer from a recent fracture or receive internal fixation. Leukocyte scan has an important diagnostic value for the patients whose osteomyelitis cannot be confirmed by bone scintigraphy. It can also be used to determine the infection in the patients who suffer from a recent fracture or receive internal fixation. PET is a fine selection for diagnosis of IAFF due to its high sensitivity and specificity and availability for patients with metallic implants, but it should not be the first choice of investigation for IAFF [9].

Serological inflammatory biomarkers

Traditional inflammatory biomarkers include white blood cell count (WBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). It is recommended that patients suspected of IAFF should receive routine WBC, ESR and CRP tests prior to treatment. The higher elevations of the three biomarkers, the greater possibility of infection. However, infection cannot be ruled out when serological levels of the three biomarkers are in normal ranges [29,30]. For patients suspected of early stage infection, repeated acquisition of CRP levels is recommended. If the serological CRP level continuously increases from the 4^{th} to 7^{th} day postoperatively, a high probability of IAFF should be considered after exclusion of infection in other systems or persistent systemic inflammatory stress status of the patient [31]. In case all the WBC, ESR and CRP levels are normal owing to the possibility of infection associated with low-virulence pathogens, or delayed and late infections, serological interleukin 6 (IL-6), tumor necrosis factor α (TNF-α) and serum amyloid A (SAA) levels can be measured for auxiliary diagnosis [30]. Potential roles of novel biomarkers, such as α-defensins, D-Dimer and calprotectin, which are more frequently used in diagnosis of PJI [32–34], in auxiliary diagnosis of IAFF need further evaluation. Currently, such novel biomarkers are not suggested for routine tests.

It should be noted that the specificity of most inflammatory biomarkers is not high enough. Elevation of such biomarkers may imply infection possibility while normal levels cannot rule out infection. A definite diagnosis should be established on the basis of clinical signs of the patient and other tests as well.

Microorganism culture and identification

As no direct relationship is found regarding pathogen culture outcomes between samples collected at the initial debridement from a contaminated wound of open fracture and IAFF samples, it is not advised to culture samples collected from an initial open fracture wound [35,36]. In order to increase the positive culture rate of samples collected during surgery in IAFF patients, it is suggested that antibiotics should not be used prior to therapy (apart from occurrence of acute infection with systemic symptoms) and antibiotics should be stopped for at least two weeks before IAFF treatment. It is not recommended to perform pathogen culture or drug sensitivity test for samples collected from a sinus tract [9,37] because the consistency percentage is low between culture outcomes from a sinus tract and intraoperative samples [38]. It is recommended that samples should be cultured for at least 7 days after collection and even for 14 days in case of suspicion of infection associated with low-virulence or specific pathogens. If necessary, cultures should be conducted for anaerobes, mycobacterium tuberculosis and fungus [3,39]. In suspicion of mature biofilm formation or in case of a negative culture outcome, the removed implant should be sent to the microbiological laboratory for sonication and cultivation of sonication fluid, in order to increase the positive culture rate [40,41]. A “3-2-1” principle is recommended for sample collection and microbiological diagnosis of IAFF. At least 3 samples from a suspected site should be collected for culture and IAFF diagnosis can be established when the same pathogens are identified from at least 2 sites. Positive culture of a high-virulence microorganism (e.g. *Staphylococcus aureus*,*Escherichia coli*) from just one site can also establish IAFF diagnosis [42]. Although polymerase chain reaction (PCR) technique possesses advantages in bacteria identification, such as convenience, efficiency, high resolution and high sensitivity, it still has such disadvantages as a false positive outcome risk owing to sample contamination, and inability to identify bacterial survival status with limited drug sensitivity information [3]. Therefore, it is not recommended as a routine test beyond its supplemental role.

Histopathological test

The histopathological test is the gold standard for diagnosis of IAFF. Therefore, all patients suspected of IAFF should receive a histopathological test of at least 2–3 samples collected intraoperatively. It is not advised to conduct an intraoperative rapid freezing histopathological test in patients with a definite preoperative IAFF diagnosis for whom a postoperative routine histopathological test is enough. However, when a surgical strategy depends on the presence or absence of infection but it is difficult to determine whether infection exists before or during surgery, rapid intraoperative freezing pathological examination is suggested of at least 2–3 soft tissue samples surrounding the suspected infected bone tissue. For tissues suspected of infection, special staining can be used to check whether pathogenic microorganisms exist under microscopy. The recommended criteria for pathological diagnosis of IAFF (including intraoperative rapid freezing pathology) should be the number of neutrophil granulocytes $\geq$5 for each of five high magnification fields (magnification ×400) [43,44].

Treatment

Active and appropriate treatment is the key to increasing the curative rate, reducing risks of infection recurrence and disability, reconstructing limb function and improving quality of life of the patient. One year follow-up in a recent study [45] demonstrated that the infection recurrence rate was as high as approximately 75% after conservative treatment. As all surgical strategies have both advantages and disadvantages [5], optimal treatment should be formulated on the basis of the personal experience of the surgeons and the specific situation of the patient. Basic principles of IAFF treatment consist of radical debridement, implant handling, systematic and local antibiotics, reconstruction of bone and soft tissue defects, and rehabilitation of limb function.

Aims of IAFF treatment and considerations for an appropriate treatment strategy [3]

Five aims should be fulfilled in the treatment of IAFF: (1) promotion of fracture consolidation, (2) eradication of infection or control of infection until fracture consolidation, (3) healing of soft-tissue coverage, (4) prevention of chronic osteomyelitis and (5) restoration of limb function.

Nine issues should be considered in selection of treatment strategies: (1) onset of infection (early, delayed or late infections), (2) fracture healing or formation of solid callus, (3) implant stability and fracture reduction, (4) implant type, (5) fracture location, (6) condition of soft tissue coverage, (7) systemic and local host physiology, (8) prior treatment of the infected site, and (9) detection of difficult-to-treat pathogens.

Radical debridement

Radical debridement is a prerequisite for IAFF treatment and also the key to a low risk of infection recurrence. In debridement, infected lesions should be treated as a low grade malignant tumor and efforts should be made to convert the bone infection which is difficult to control into bone defects that can be repaired [46]. The key point in debridement is to clear away all the necrotic and deactivated bone and soft tissue. *Oncologic resection* is recommended as the standard manner of debridement, which exceeds 5 mm into normal tissues [3,47]. "*Paprika sign*" of bone and soft tissue is a criterion for radical debridement which can be assisted by devices like water jet and pulse irrigator. Debridement of reamer-irrigator-aspirator (RIA) style is recommended for intramedullary infection [48]. When acute infection is highly suspected following internal fixation, active surgical intervention is advised rather than conservative observation. It is mandatory to open the wound in time, perform radical debridement and delay wound closure. Negative pressure wound therapy can be applied when necessary and antimicrobial-coated sutures (e.g. triclosan) can be used for wound closure [49].

Implant handling

Currently, there has been no evidence-based suggestion regarding whether to keep or remove the implant after acute infection (<2 weeks). It is generally recommended to keep the implant as long as fracture achieves satisfactory reduction, hardware remains stable and infection is effectively controlled. However, the implant should be removed in cases of (1) a patient addicted to drug or smoking, (2) compromised immunity which cannot recover in a short time, (3) open fracture, (4) intramedullary fixation, (5) unsatisfactory fracture reduction or unstable fixation, (6) poor soft tissue condition or insufficient wound coverage, and (7) bacterial infection difficult to treat (e.g. methicillin-resistant *staphylococcus aureus*, MRSA) [3,50]. For delayed infection (2∼10 weeks), the implant should be kept only on condition that fracture reduction is fine, internal fixation rigid, infection effectively controlled and coverage of soft tissue sufficient. In case of chronic infection (>10 weeks), the implant can be removed after the fracture has already healed. In ununited fractures, the implant should be handled the same way as for delayed infection.

A decision to keep the implant in place should be cautiously made no matter at which stage the infection is. Patients with the implant retained should be watched out for clinical symptoms and given antibiotics and supportive therapies. Dynamic tests of serological levels of inflammatory biomarkers are suggested, especially CRP. Once CRP level increases continuously with aggravated systemic and/or local symptoms of inflammation, the implant should be removed in time not to aggravate bone infection.

Systemic antibiotic treatment

Systematic antibiotic treatment aims to have either curative or suppressive effects. If suppression is aimed at, antibiotics should be administered to control infection until the fracture unites and the implant can be removed [4]. Antibiotics should be chosen according to the results of intraoperative sample cultures and antimicrobial susceptibility tests. The most frequently used antibiotics are cephalosporin and clindamycin [45]. Antibiotic treatment should start immediately after radical debridement, and intravenous administration for 2 weeks followed by oral administration [51,52] is recommended. If curative effects are aimed at, antibiotics should continue for 6 weeks (intravenous administration for 2 weeks followed by oral administration for 4 weeks) after implant removal. However, duration of antibiotics should be prolonged to 12 weeks if the implant is retained (intravenous administration for 2 weeks followed by oral administration for 10 weeks) [4,53]. As duration of systemic antibiotics associates with the time for stabilization and fracture union in case of suppression, additional 4–6 weeks after implant removal are usually required, especially for infection induced by high-virulent bacteria. Vancomycin or daptomycin can be selected in suspicion of MRSA-related infection [54]. For delayed or chronic infection where a bacterial biofilm forms, rifampicin [55] and quinolones (ciprofloxacin, levofloxacin) [56,57] should be supplemented after surgical debridement for infection related to staphylococcus and gram-negative bacteria, respectively. Postoperative use of mere rifampicin is not suggested for it may result in rapid development of resistance. Instead, rifampicin should be used in combination with other broad-spectrum antibiotics [58].

Local antibiotic implantation

Local application of antibiotics requires vehicles. Currently, the carriers most frequently used are polymethylmethacrylate (PMMA) and calcium sulfate (CS). Antibiotics that can be locally implanted include vancomycin, gentamicin, tobramycin and cephalosporin [59]. Local use of antibiotic-loaded carriers should follow radical debridement of the infected tissues. Patients should be fully informed of both advantages and disadvantages of different types of antibiotic carrier. For example, although PMMA can provide adequate support strength, it is not biodegradable and requires a secondary removal surgery. CS is completely biodegradable, but aseptic wound drainage is a frequent complication following local implantation [60,61].

Reconstruction of bone defects

Radical debridement of osseous tissue usually causes a bone defect. Autogenous bone graft, myocutaneous flap and fasciocutaneous flap

can be chosen to repair bone defects smaller than 4∼6 cm. With regard to large bone defects (over 4∼6 cm), Ilizarov, Masquelet and free vascularized fibula graft techniques can be applied. Since all techniques have their own advantages and disadvantages, surgeons should choose an optimal technique based on their personal experience and specific patient situation.

Illizarov distraction osteogenesis technique (Bone transport technique) [62]

Key points of Illizarov technique are metaphyseal osteotomy and lower-energy osteotomy to protect blood supply. Bone transport usually starts one week following osteotomy (range, 3–10 days) at a speed of 1.0 mm/d (range, 0.5–1.5 mm/d) fulfilled at 3–4 times. The first stage osteotomy can be performed after debridement in patients with slight or moderate infection. The second stage osteotomy should be considered in cases of severe infection, transport planned from distal to proximal limb and poor patient status. It is usually conducted 4 to 6 weeks following primary surgery. Dynamic observation of serological levels of inflammatory biomarkers (especially CRP) is necessary. It is safer to perform osteotomy when CRP level returns to normal. A rail fixator is the first choice for bone transport. Ring fixators, being more stable than rail ones, can be considered when rail fixators cannot provide rigid fixation [63], or when osteotomy site is close to joint surface (a rail fixator nail implanted may penetrate into the joint). Routine freshening of the docking sites with bone graft is not recommended. Nonetheless, such surgical procedures can be considered if no obvious or little callus forms 2–3 months following docking sites contact or if re-fracture risk significantly increases after removal of external fixation. If a patient cannot tolerate long-term wear of an external fixator, early bone graft and exchange into internal fixation can be considered [64] as long as infection has been completely eradicated.

Masquelet technique (the induced membrane technique) [65]

Masquelet technique is an effective strategy to deal with large segmental bone defects [66]. It is strongly recommended that surgeons should strictly follow the surgical points at each stage in order to avoid surgical failure (including changing surgical procedures at any stage) [67,68]. The primary technical points in the first stage surgery include radical debridement of bone and soft tissue, implantation of PMMA cement into bone defects (cement filling should wrap the defect ends by 2–3 cm), good soft tissue coverage and rigid fixation of fracture ends. The second stage surgery is usually conducted 6–8 weeks after the first stage one. Dynamic tests of serological levels of inflammatory biomarkers prior to the second stage surgery are necessary. The secondary stage surgery can be performed when serological levels of inflammatory biomarkers return to normal or almost normal. As a primary technical point in the second stage surgery, the block of cement spacer must be removed without dissecting the membrane from its surrounding tissues. Bacterial culture and histopathological examination should be carried out in suspicion of residual infection. After removal of the cement spacer, bone defect ends need to be refreshed and the medullar cavities at both ends should be reamed. Next, the defect is filled up with autograft bone. Allograft bone and bone graft substitutes can be used for massive bone defects. It should be noted the volume ratio of autogenous bone to allogeneic filling should exceed 3:1. Subsequently, terminal fixation is applied as appropriately as the circumstances may require. The membrane is sutured over the graft with adherent soft tissues. It is advised to put drainage inside the cavity of membrane or in the subcutaneous tissue.

Free vascularized fibular graft technique

Free vascularized fibular graft, a technique most frequently used to reconstruct bone defects [69,70], requires well-experienced micro-surgeons. Since it takes a long time for the fibular graft to thicken, regular follow-ups are essential to reduce risks of refracture and other complications [71].

Repair of soft tissue defects

Since a good soft tissue condition is essential for effective control of infection, soft tissue defects should be repaired as soon as possible in any surgical strategy. Soft tissue defects in an open fracture should also be covered as soon as possible (within 1 week after injury). They can be repaired by a free or local flap, musculocutaneous flap, skin graft and skin stretching technique.

Rehabilitation of limb function

Rehabilitation should be encouraged no matter which surgery has been performed so that incidences of osteoporosis, ankylosis, foot-drop and other complications can be reduced. A rehabilitation strategy should be personalized based on specific patient situation and treatment method, in order to speed up the recovery of the patient and improve his or her quality of life.

Summary and prospects

Diagnosis and treatment of IAFF is always a great concern and a difficult problem as well for orthopaedists. Although remarkable advances have been achieved in relative fields, many aspects of the disorder are still unclear or in controversy. The standards and criteria that have been formulated for diagnosis and treatment of IAFF are derived from those for PJI. Therefore, extensive, in-depth and meticulous clinical and basic investigations of IAFF are necessary. We hope IAFF patients may benefit more from multidisciplinary collaboration in the future [72]. Their quality of life can be improved and their risks of recurrence and disability can be reduced by progress in early diagnosis and appropriate treatment of IAFF and in preventive medicine which allows for precise identification of high-risk populations of IAFF and timely effective intervention to lower prevalence of IAFF.

Experts participated in the consensus statement

Wei-jun An, Zheng-gang Bi, Shan-bao Cai, Xian-hua Cai, Rui-zhi Cao, Xue-cheng Cao, Yang Cao, Bing-fang Zeng, Yi-min Chai, Hua Chen, Ai-min Chen, Hua Chen, Shun-you Chen, Wei Chen, Wei-gao Chen, Yan-xi Chen, Yun-zhen Chen, Zhong Chen, Peng Cheng, Lei-ting Chi, Xiao-qian Dang, Xue-feng Deng, Zhen-qi Ding, Jing-ming Dong, Guo-feng Fan, Shi-yuan Fang, Wei Feng, Xiao-bing Fu, Zhong-guo Fu, Peng Gao, Qiu-ming Gao, Li-qiang Gu, Jian-zhong Guan, Rong-guang Guo, Xiao-shan Guo, Yang Guo, Zhi-yong Hou, Yan-jun Hu, Fu-guo Huang, Lei Huang, Hong-quan Ji, Fang Ji, Shi-kong Jia, Yan-fei Jia, Bao-guo Jiang, Guang-cai Jiang, Xie-yuan Jiang, Yu-hua Jing, Qing-lin Kang, Rong Kong, Jun Li, Kai-nan Li, Lin-qi Li, Wei-xu Li, Zhong Li, Du Liang, Jia-li Liang, Qi Liao, Feng-fei Lin, Peng Lin, Zhang-yuan Lin, Fan Liu, Yong Liu, Zhi Liu, Guang-yao Liu, Guo-hui Liu, Lei Liu, Li-jun Liu, Li-min Liu, Xi-ming Liu, Ya-ke Liu, Zhi-xiang Liu, Hao Liu, Cong-feng Luo, Gang Luo, Xin Lv, De-cheng Lv, Gang Lv, Zhi Lv, Bao-tong Ma, Xian-zhong Ma, Xin-long Ma, Jiang-dong Ni, Wei-dong Ni, Zhi-jun Pan, Guo-xian Pei, A-qin Peng, Jian Qi, Hong-bo Qian, Yi-jun Ren, Yong-jun Rui, Xi-guang Sang, Jian Shang, Lin Shao, Zhan-ying Shi, Qing-xuan Shi, Shi-qin Shi, Heng-sheng Shu, Chao-hui Song, Wen-chao Song, Wei Su, Da-hui Sun, Hai-yu Sun, Hong-tao Sun, Jia-bing Sun, Yu-qiang Sun, Yue-hua

Sun, Cheng-he Qin, Wen-fu Tan, Xin Tang, Jian Tang, Pei-fu Tang, Ran Tao, Xing Teng, Yun Tian, Da-ke Tong, Yu-liang Wang, Dong Wang, Gang Wang, Ai-guo Wang, Bao-jun Wang, Guang-lin Wang, Guo-xuan Wang, Lei Wang, Li-min Wang, Man-yi Wang, Peng-cheng Wang, Qiu-gen Wang, Wan-ming Wang, Xin-wei Wang, Yue Wang, Zheng-guo Wang, Zheng-yuan Wang, Liang-yuan Wen, Bo Wu, Dan-kai Wu, Duo-qing Wu, Ke-jian Wu, Li-sheng Wu, Xin-bao Wu, Zheng-jie Wu, De-ming Xiao, Zhao Xie, Zeng-ru Xie, Ming Xu, Wei-guo Xu, Yong-qing Xu, Jun Yang, Lei Yang, Hua-qing Yang, Ming-hui Yang, Sheng-song Yang, Qi Yao, Fa-gang Ye, Jun-jian Ye, Peng Ye, Bin Yu, Bao-qing Yu, Zhi Yuan, Kun Zhang, Yi Zhang, Bao-zhong Zhang, Dian-ying Zhang, Jian-ning Zhang, Jian-zheng Zhang, Jin-li Zhang, Li-hai Zhang, Qun Zhang, Shu-ming Zhang, Wei Zhang, Ya-kui Zhang, Ying-ze Zhang, Chang-qing Zhang, Jin-min Zhao, Wen Zhao, Zhe Zhao, Long-po Zheng, Fang Zhou, Dong-sheng Zhou, Jun-lin Zhou, Yong Zhu, Shi-wen Zhu, Yong-zhan Zhu, Yue-liang Zhu, Yan Zhuang, Yun-qiang Zhuang.

Chinese Expert Consensus on Diagnosis and Treatment of Infection after Fracture Fixation (2018 Edition).

Acknowledgement

The authors thanks Prof. Allen P. Liang for language revision and editing.

References

[1] Metsemakers WJ, Kortram K, Morgenstern M, Moriarty TF, Meex I, Kuehl R, et al. Definition of infection after fracture fixation: a systematic review of randomized controlled trials to evaluate current practice. Injury 2018;49:497–504.
[2] Morgenstern M, Moriarty TF, Kuehl R, Richards RG, McNally MA, Verhofstad MHJ, et al. International survey among orthopaedic trauma surgeons: lack of a definition of fracture-related infection. Injury 2018;49:491–6.
[3] Metsemakers WJ, Kuehl R, Moriarty TF, Richards RG, Verhofstad MHJ, Borens O, et al. Infection after fracture fixation: current surgical and microbiological concepts. Injury 2018;49:511–22.
[4] Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. Injury 2006;37(Suppl. 2):S59–66.
[5] Panteli M, Giannoudis PV. Chronic osteomyelitis: what the surgeon needs to know. EFORT Open Rev 2016;1:128–35.
[6] Cierny 3rd G, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res 2003;7–24.
[7] Jiang N, Qin CH, Yu B. Advances in diagnosis and treatment of infection after internal fixation. Chin J Orthop Trauma 2015;17:764–9.
[8] Zimmerli W. Clinical presentation and treatment of orthopaedic implant-associated infection. J Intern Med 2014;276:111–9.
[9] Morgenstern M, Kuhl R, Eckardt H, Acklin Y, Stanic B, Garcia M, et al. Diagnostic challenges and future perspectives in fracture-related infection. Injury 2018;49(Suppl. 1):S83–90.
[10] Hogan A, Heppert VG, Suda AJ. Osteomyelitis. Arch Orthop Trauma Surg 2013;133:1183–96.
[11] Momaya AM, Hlavacek J, Etier B, Johannesmeyer D, Oladeji LO, Niemeier TE, et al. Risk factors for infection after operative fixation of Tibial plateau fractures. Injury 2016;47:1501–5.
[12] Parkkinen M, Madanat R, Lindahl J, Makinen TJ. Risk factors for deep infection following plate fixation of proximal tibial fractures. J Bone Joint Surg Am 2016;98:1292–7.
[13] Zhu Y, Liu S, Zhang X, Chen W, Zhang Y. Incidence and risks for surgical site infection after adult tibial plateau fractures treated by ORIF: a prospective multicentre study. Int Wound J 2017;14:982–8.
[14] Korim MT, Payne R, Bhatia M. A case-control study of surgical site infection following operative fixation of fractures of the ankle in a large U.K. trauma unit. Bone Joint J 2014;96-B:636–40.
[15] Olsen LL, Moller AM, Brorson S, Hasselager RB, Sort R. The impact of lifestyle risk factors on the rate of infection after surgery for a fracture of the ankle. Bone Joint J 2017;99B:225–30.
[16] Sagi HC, Donohue D, Cooper S, Barei DP, Siebler J, Archdeacon MT, et al. Institutional and seasonal variations in the incidence and causative organisms for posttraumatic infection following open fractures. J Orthop Trauma 2017;31:78–84.
[17] Claessen FM, Braun Y, van Leeuwen WF, Dyer GS, van den Bekerom MP, Ring D. What factors are associated with a surgical site infection after operative treatment of an elbow fracture? Clin Orthop Relat Res 2016;474:562–70.
[18] Marais LC, Ferreira N, Aldous C, Sartorius B, Le Roux T. A modified staging system for chronic osteomyelitis. J Orthop 2015;12:184–92.
[19] Tseng CH, Huang WS, Muo CH, Chang YJ, Sung FC. Increased risk of intracerebral hemorrhage among patients with chronic osteomyelitis. J Neurosurg 2015;123:1528–33.
[20] Lai SW, Lai HC, Lin CL, Liao KF, Tseng CH. Chronic osteomyelitis correlates with increased risk of acute pancreatitis in a case-control study in Taiwan. Eur J Intern Med 2015;26:429–32.
[21] Hsiao LC, Muo CH, Chen YC, Chou CY, Tseng CH, Chang KC. Increased risk of coronary heart disease in patients with chronic osteomyelitis: a population-based study in a cohort of 23 million. Heart 2014;100:1450–4.
[22] Lin SY, Lin CL, Tseng CH, Wang IK, Wang SM, Huang CC, et al. The association between chronic osteomyelitis and increased risk of diabetes mellitus: a population-based cohort study. Eur J Clin Microbiol Infect Dis 2014;33:1647–52.
[23] Tseng CH, Huang WS, Muo CH, Chang YJ, Kao CH. Increased depression risk among patients with chronic osteomyelitis. J Psychosom Res 2014;77:535–40.
[24] Metsemakers WJ, Smeets B, Nijs S, Hoekstra H. Infection after fracture fixation of the tibia: analysis of healthcare utilization and related costs. Injury 2017;48:1204–10.
[25] Jiang N, Wu H, Lin Q, Hu Y, Yu B. Direct healthcare costs and utilization for inpatients with extremity post-traumatic osteomyelitis: a retrospective single-center observational study in Southern China. 37th Annual Meeting of the European Bone and Joint Infection Society. .
[26] Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, et al. Fracture-related infection: a consensus on definition from an international expert group. Injury 2018;49:505–10.
[27] Pineda C, Espinosa R, Pena A. Radiographic imaging in osteomyelitis: the role of plain radiography, computed tomography, ultrasonography, magnetic resonance imaging, and scintigraphy. Semin Plast Surg 2009;23:80–9.
[28] Lee YJ, Sadigh S, Mankad K, Kapse N, Rajeswaran G. The imaging of osteomyelitis. Quant Imaging Med Surg 2016;6:184–98.
[29] Stucken C, Olszewski DC, Creevy WR, Murakami AM, Tornetta P. Preoperative diagnosis of infection in patients with nonunions. J Bone Joint Surg Am 2013;95:1409–12.
[30] Jiang N, Qin CH, Hou YL, Yao ZL, Yu B. Serum TNF-α, ESR and IL-6 are more valuable biomarkers for assisted diagnosis of extremity chronic osteomyelitis. Biomark Med 2017;11:597–605.
[31] Fang C, Wong TM, Lau TW, To KK, Wong SS, Leung F. Infection after fracture osteosynthesis - part I. J Orthop Surg (Hong Kong) 2017;25:2309499017692712.
[32] Gehrke T, Lausmann C, Citak M, Bonanzinga T, Frommelt L, Zahar A. The accuracy of the alpha defensin lateral flow device for diagnosis of periprosthetic joint infection: comparison with a gold standard. J Bone Joint Surg Am 2018;100:42–8.
[33] Shahi A, Kheir MM, Tarabichi M, Hosseinzadeh HRS, Tan TL, Parvizi J. Serum D-Dimer test is promising for the diagnosis of periprosthetic joint infection and timing of reimplantation. J Bone Joint Surg Am 2017;99:1419–27.
[34] Wouthuyzen-Bakker M, Ploegmakers JJW, Kampinga GA, Wagenmakers-Huizenga L, Jutte PC, Muller Kobold AC. Synovial calprotectin: a potential biomarker to exclude a prosthetic joint infection. Bone Joint J 2017;99-B:660–5.
[35] Valenziano CP, Chattar-Cora D, O'Neill A, Hubli EH, Cudjoe EA. Efficacy of primary wound cultures in long bone open extremity fractures: are they of any value? Arch Orthop Trauma Surg 2002;122:259–61.
[36] Burns TC, Stinner DJ, Mack AW, Potter BK, Beer R, Eckel TT, et al. Microbiology and injury characteristics in severe open tibia fractures from combat. J Trauma Acute Care Surg 2012;72:1062–7.
[37] Aggarwal VK, Higuera C, Deirmengian G, Parvizi J, Austin MS. Swab cultures are not as effective as tissue cultures for diagnosis of periprosthetic joint infection. Clin Orthop Relat Res 2013;471:3196–203.
[38] Soomro S, Siddiqi MA, Taufiq I. Diagnostic value of sinus tract culture versus intraoperative bone culture in patients with chronic osteomyelitis. J Pak Med Assoc 2016;66(Suppl. 3):S109–11.
[39] Sheehy SH, Atkins BA, Bejon P, Byren I, Wyllie D, Athanasou NA, et al. The microbiology of chronic osteomyelitis: prevalence of resistance to common empirical anti-microbial regimens. J Infect 2010;60:338–43.
[40] Yano MH, Klautau GB, da Silva CB, Nigro S, Avanzi O, Mercadante MT, et al. Improved diagnosis of infection associated with osteosynthesis by use of sonication of fracture fixation implants. J Clin Microbiol 2014;52:4176–82.
[41] Puig-Verdie L, Alentorn-Geli E, Gonzalez-Cuevas A, Sorli L, Salvado M, Alier A, et al. Implant sonication increases the diagnostic accuracy of infection in patients with delayed, but not early, orthopaedic implant failure. Bone Joint J 2013;95-b:244–9.
[42] Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013;56: e1-e25.
[43] Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res 2011;469:2992–4.
[44] Morgenstern M, Athanasou NA, Ferguson JY, Metsemakers WJ, Atkins BL, McNally MA. The value of quantitative histology in the diagnosis of fracture-related infection. Bone Joint J 2018;100-B:966–72.
[45] Jiang N, Ma YF, Jiang Y, Zhao XQ, Xie GP, Hu YJ, et al. Clinical characteristics and treatment of extremity chronic osteomyelitis in Southern China: a retrospective analysis of 394 consecutive patients. Medicine (Baltimore) 2015;94:e1874.
[46] Patzakis MJ, Zalavras CG. Chronic posttraumatic osteomyelitis and infected nonunion of the tibia: current management concepts. J Am Acad Orthop Surg 2005;13:417–27.

[47] Simpson AH, Deakin M, Latham JM. Chronic osteomyelitis. The effect of the extent of surgical resection on infection-free survival. J Bone Joint Surg Br 2001;83:403–7.
[48] Zalavras CG, Sirkin M. Treatment of long bone intramedullary infection using the RIA for removal of infected tissue: indications, method and clinical results. Injury 2010;41(Suppl. 2):S43–47.
[49] Wu X, Kubilay NZ, Ren J, Allegranzi B, Bischoff P, Zayed B, et al. Antimicrobial-coated sutures to decrease surgical site infections: a systematic review and meta-analysis. Eur J Clin Microbiol Infect Dis 2017;36:19–32.
[50] Mouzopoulos G, Kanakaris NK, Kontakis G, Obakponovwe O, Townsend R, Giannoudis PV. Management of bone infections in adults: the surgeon's and microbiologist's perspectives. Injury 2011;42(Suppl. 5):S18–23.
[51] Spellberg B, Lipsky BA. Systemic antibiotic therapy for chronic osteomyelitis in adults. Clin Infect Dis 2012;54:393–407.
[52] Rod-Fleury T, Dunkel N, Assal M, Rohner P, Tahintzi P, Bernard L, et al. Duration of post-surgical antibiotic therapy for adult chronic osteomyelitis: a single-centre experience. Int Orthop 2011;35:1725–31.
[53] Schmidt AH, Swiontkowski MF. Pathophysiology of infections after internal fixation of fractures. J Am Acad Orthop Surg 2000;8:285–91.
[54] Jiang N, Qin CH, Yu B. Current antibiotic treatment options for fracture implant-associated infection. Orthop J China 2015;23:1489–92.
[55] Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group. JAMA 1998;279:1537–41.
[56] Hsieh PH, Lee MS, Hsu KY, Chang YH, Shih HN, Ueng SW. Gram-negative prosthetic joint infections: risk factors and outcome of treatment. Clin Infect Dis 2009;49:1036–43.
[57] Aboltins CA, Dowsey MM, Buising KL, Peel TN, Daffy JR, Choong PF, et al. Gram-negative prosthetic joint infection treated with debridement, prosthesis retention and antibiotic regimens including a fluoroquinolone. Clin Microbiol Infect 2011;17:862–7.
[58] Achermann Y, Eigenmann K, Ledergerber B, Derksen L, Rafeiner P, Clauss M, et al. Factors associated with rifampin resistance in staphylococcal periprosthetic joint infections (PJI): a matched case-control study. Infection 2013;41:431–7.
[59] ter Boo GJ, Grijpma DW, Moriarty TF, Richards RG, Eglin D. Antimicrobial delivery systems for local infection prophylaxis in orthopedic- and trauma surgery. Biomaterials 2015;52:113–25.
[60] Ferguson JY, Dudareva M, Riley ND, Stubbs D, Atkins BL, McNally MA. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis A SERIES OF 195 CASES. Bone Joint J 2014;96B:829–36.
[61] McNally MA, Ferguson JY, Lau AC, Diefenbeck M, Scarborough M, Ramsden AJ, et al. Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate/hydroxyapatite biocomposite: a prospective series of 100 cases. Bone Joint J 2016;98-B:1289–96.
[62] Ilizarov GA. The principles of the Ilizarov method. Bull Hosp Jt Dis Orthop Inst 1988;48:1–11.
[63] Rohilla R, Wadhwani J, Devgan A, Singh R, Khanna M. Prospective randomised comparison of ring versus rail fixator in infected gap nonunion of tibia treated with distraction osteogenesis. Bone Joint J 2016;98-B:1399–405.
[64] Zhang ST, Wang H, Zhao JJ, Xu P, Shi H, Mu WD. Treatment of post-traumatic chronic osteomyelitis of lower limbs by bone transport technique using mono-lateral external fixator: follow-up study of 18 cases. J Orthop Sci 2016;21:493–9.
[65] Masquelet AC, Fitoussi F, Begue T, Muller GP. Reconstruction of the long bones by the induced membrane and spongy autograft. Ann Chir Plast Esthet 2000;45:346–53.
[66] Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romano CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury 2016;47(Suppl. 6):S68–76.
[67] Masquelet AC. Induced membrane technique: pearls and pitfalls. J Orthop Trauma 2017;31(Suppl. 5):S36–8.
[68] Mauffrey C, Hake ME, Chadayammuri V, Masquelet AC. Reconstruction of long bone infections using the induced membrane technique: tips and tricks. J Orthop Trauma 2016;30:e188–193.
[69] Le Thua TH, Pham DN, Boeckx W, De Mey A. Vascularized fibular transfer in longstanding and infected large bone defects. Acta Orthop Belg 2014;80:50–5.
[70] Gao-Hong R, Run-Guang L, Gui-Yong J, Chao-Jie C, Zhi-Gang B. A solution to the vessel shortage during free vascularized fibular grafting for reconstructing infected bone defects of the femur: bridging with vein transplantation. Injury 2017;48:486–94.
[71] Kovoor CC, Jayakumar R, George V, Padmanabhan V, Guild A, Viswanath S. Vascularized fibular graft in infected tibial bone loss. Indian J Orthop 2011;45:330–5.
[72] Bose D, Kugan R, Stubbs D, McNally M. Management of infected nonunion of the long bones by a multidisciplinary team. Bone Joint J 2015;97-B:814–7.