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Acute and chronic infection: Is there a gold standard for management of the wound and bone defect?

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Abstract

Acute and chronic infections with bone involvement remain a challenge to manage. They pose a significant burden to the patient, the treating surgeon, and society. Multidisciplinary team involvement is mandatory for a successful outcome. Application of a gold standard approach is not possible due to the high heterogeneous patient population and the variable degree of severity of soft tissue and bone involvement. The mainstay of treatment remains the conversion of a septic environment to an aseptic one with aggressive debridement of the affected soft tissues and bone. Reconstruction of the soft tissue defect can be achieved using modern microsurgical techniques, whereas the induced membrane and distraction osteogenesis (bone transport) are currently the 2 most commonly used treatment modalities for bone loss.

The safest approach to deal successfully with this multifaceted clinical pathology is to always follow well-established principles of management and adapt treatment to the personalized needs of the patient.

Keywords: bone defect, bone infection, debridement, osteomyelitis

1. Introduction

The management of acute and chronic infections poses a significant burden to the patient, the treating surgeon, and society. The infectious process may start from the superficial soft tissues (as cellulitis; abscess formation), and eventually with time, if left untreated, can propagate to the bone. A prolonged bone infection leads to the establishment of chronic osteomyelitis.[1]

Nowadays, it is well accepted that the treatment of bone infection requires a lengthy time in the vast majority of cases, demands special skills and expertise of the surgeon, includes multiple operating procedures, necessitates the involvement of multiple specialties, and is costly. Interestingly, parameters that can affect the establishment, chronicity, and outcome of management of infection include the initial severity of soft tissue and bone injury sustained (i.e., open fractures), the profile of the patient (age, immune status, presence of comorbidities, medication intake), and the timing and the quality of care provided by the surgical team.[2] It therefore becomes apparent that the management and clinical course of these patients is challenging and since so many factors have an important role to play, the outcome could be unpredictable.

However, one may question whether it is possible to apply a "gold standard" of treatment for the management of this patient cohort. The definition of gold standard implies "a thing of superior quality which serves as a point of reference against which other things of its type may be compared." Consequently, we will examine the issues and challenges associated with the management of acute and chronic infection and examine whether a gold standard of treatment can be applied.

1.1. Management of wound and bone defect

When infection has been established, it is essential to identify the extent of the problem, the pathogen responsible for the infectious process and to work out a plan to achieve an aseptic local environment, prior to considering restoration of both the soft tissue and bone that might be missing as a result of the debridement carried out. It is imperative to become familiar with the natural history of the presenting complaint. For instance, the severity of the initial injury sustained in terms of wound size and extent of contamination, bone involvement (degree of initial bone loss), type of fixation used, and subsequent clinical course of the patient. The clinician must become aware about the number of previous procedures carried out, any episodes of infection, and length of chronicity of the problem. Information relevant to the patient's profile (comorbidities, medication, smoking habits, vitamin D levels, etc) is also essential. Diagnostic investigations aiming to provide information in relation to the extent of soft tissue and bone infection involvement include, ultra sound (U/S), plain radiographs, computerized tomography scan, magnetic resonance imaging, and positron emission tomography scan.[3–5]

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Hematological investigations will provide base line levels of infection markers (WBC, CRP, ESR) for subsequent monitoring of the success of treatment implemented.

Overall, the management involves the excision of the infected bone along with the infected soft tissues and the administration of culture-specific antibiotics. The removal of the unhealthy soft tissue and underlying necrotic bone, results in a soft tissue and bone defect that needs to be addressed by the treating surgeon. Taking into consideration the contribution and importance of all the above parameters discussed, it can be argued that the patient population and clinical problem of acute and chronic infection is highly "heterogeneous" with a very broad spectrum of severity. Consequently, it is the author's opinion that there is no gold standard for the management of the wound and bone defect. The safest approach to deal successfully with this multifaceted clinical pathology is to always follow well-established principles of management and adapt treatment to the personalized needs of the patient. Moreover, the involvement of a multidisciplinary team (orthopaedic surgeon, radiologist, plastic surgeon, microbiologist, physiotherapist, etc) is mandatory for a successful outcome.

For the soft tissue management, the principles of treatment are based on the following aims: conversion of a contaminated wound into a clean one, conversion of a devascularized wound into a vascularized one, and finally closure of the clean, tidy vascularized wound, thus promoting healthy wound healing with a very low risk of development of infection. In cases where extensive soft tissue loss has resulted, soft tissue reconstruction in the form of a rotational muscle flap, or free tissue muscle transfer using microvascular techniques is required. Different microsurgical techniques can be applied based on the location of the soft tissue defect, the size of the defect, and presence or absence of other ipsilateral limb injuries.

Management of the infected bone can be challenging. Up to recently and due to the lack of well-developed microsurgical techniques and the reconstruction of soft tissues with free vascularized flaps, amputation was a common solution for infected long bones.[6]

Noteworthy, even now, it is difficult to identify accurately the margins of bone that remain free of infection. Radiological investigations can be inconclusive and consequently it comes down to the experience and the skills of the surgeon to remove successfully all the infected bone tissue. Aggressive debridement away from the zone of injury is essential. The surgeon should not worry about the length of the bone defect to be created secondary to the excision process. Indeed, modern techniques of bone reconstruction can repair defects as long as 25 cm in length.[7]

1.2. The critical bone defect

Despite the fact that there is significant clinical and laboratory research in the field of bone defects, there is no consensus amongst orthopaedic surgeons regarding the definition of the "critical sized bone defect."[8] A simplistic definition defines the critical defect as the one that will not heal without additional surgical intervention. Evidence from animal and human studies suggests that defects more than 2.5 cm have a guarded prognosis and heal with difficulty, thus necessitating further surgical intervention. It has also been proposed that a critical bone defect is the one with a segmental bone deficit of a length exceeding 2–2.5 times the diameter of the affected bone.[9]

The anatomic site of the defect, with tibial defects having possibly the worst prognosis, plays a significant role in the end result of union. Other parameters that should be considered in the characterization of a defect as critical are the patients' age and the presence of comorbidities and systemic disorders that affect the bone healing process, for example, smoking, malnutrition, autoimmune diseases, etc.[10]

Nowadays, the available options to manage bone defects include the induced membrane technique, distraction osteogenesis, implantation of titanium cages, prosthetic replacement, vascularized fibula allografts, and lately the intramedullary lengthening devices.[8] The answer to the question of which method is better and whether indeed there is a gold standard is very difficult since the quality of the published data is low and the outcome of the method used is predicated upon the surgeons expertise and experience. Nevertheless, the overwhelming literature comes from the induced membrane (Masquelet) technique and the distraction osteogenesis (Ilizarov) method.

1.3. The induced membrane technique

The Masquelet technique was first introduced in the early 1990s and has revolutionized the treatment of infected and noninfected (traumatic, due to tumor resection) long-bone defects.[10] Currently, its use for the treatment of an infection has become one of the most common methods worldwide (Figs. 1–4). It is a 2-staged procedure that requires a robust preoperative assessment of the patient and planning of the surgical procedures. The steps of the method along with the specific technical details have been well described.[11] Nevertheless, the majority of the existing clinical studies of the technique are retrospective in their design.[10] Three retrospective clinical studies[12–14] provided the best date available up to date. In 2012, Krager et al[12] published the largest retrospective series that included 84 posttraumatic long bone defects out of which 41 had an infection. Giannoudis et al[13] described a single-center experience of 21 patients with infected nonunion or underlying osteomyelitis that were treated with the Masquelet technique. Twenty of these patients went to solid union at a mean time of 5.6 months (range 2–10 months) after the initiation of treatment with an average time to healing of 1.21 months per centimeter of defect. This represents a success rate of 95.23% (20 in 21 cases) of the technique. In all patients the PMMA used during the first stage was enriched with antibiotics and at the second stage the "diamond concept,"[15] that is favorable mechanical environment, presence of adequate cellular populations, inductive stimulating proteins, osteoconductive matrix, and vascularity, was applied. In 2017, Qiu et al[14] retrospectively reviewed 40 patients of posttraumatic osteomyelitis of the tibia that were treated with the Masquelet technique. For the management of the dead space after the initial debridement the authors used antibiotic-impregnated cement beads (18 patients) or spacers (22 patients). The authors concluded that the spacers and the beads have equivalent results in the management of posttraumatic osteomyelitis and that spacers are not suitable for the management of large/segmental bone defects. In the only known to us prospective study, Cho et al[16] included 21 patients who were treated with the Masquelet technique. In a case series of 19 patients, debridement of infection (12 posttraumatic osteomyelitis, 4 infected nonunion, and 3 chronic osteomyelitis) was the reason for the implementation of the technique. The authors introduced a circumferential bone graft around an absorbable gelatin sponge core and used the induced membrane technique. Most of the patients had large bone defects and multiple previous surgical interventions; 4.1 previous operations (range, 2–11 failures) among the 19 cases of osteomyelitis and infected

Figure 1. (A) AP and (B) lateral radiographs of left forearm in a 28-year-old male with an infected ulna nonunion. The fracture had been fixed 4 months previously in a local hospital, and the plate was removed due to the infection.

nonunions. Most of the patients also had more than 1 debridement prior to the graft application. The overall success (union) rate was reported to be 85.71% (18 in 21 cases).

The induced membrane technique is a relatively new method in the treatment of bone defects. New substantial experience is gained in the clinical setting and more knowledge is acquired from laboratory studies constantly. As the method is ever evolving questions are generated and should be studied. The role of the age of the patient in the outcome of the method, the maximum length, and volume of the defect that can be treated with the method, the best type of cement that induces the optimal quality membrane, the ideal timing for the second stage, the best composition of the grafting material and the ideal osteosynthesis construct are the contemporary unanswered questions that we need to address in the near future.[10]

1.4. Distraction osteogenesis

Distraction osteogenesis is a method of bone regeneration which after its introduction in the Western World in the mid-1980s has now come into maturity and its being used by orthopaedic trauma surgeons with substantial success. In the case of infected nonunions and osteomyelitis, it involves the removal of the affected bone and soft tissues to a grossly healthy area, the application of a circular frame, and the gradual transportation of a segment of bone into the area of the bone deficit. The bone segment is created by a metaphyseal corticotomy and the transportation is applied after a latency period. The area of the corticotomy is called the "regenerate site" and the area where the union of the moving segment and the stationary segment must occur is called the "docking area." The success of the method in the management of closed and open tibial fractures has been well documented. In a retrospective case series of their practice, Foster

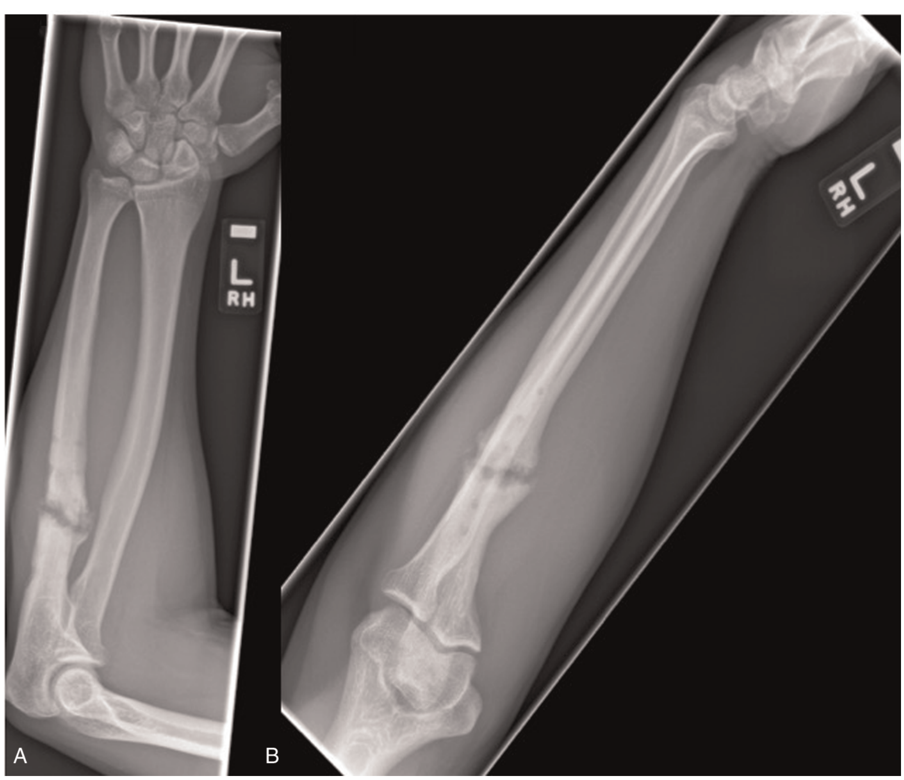

Figure 2. (A) AP and (B) lateral radiographs at 6-month follow-up when the patient (also shown in fig. 1) was referred to our institution for further management. Radiographs demonstrated advanced bone resorption at the nonunion site secondary to the underlying infection (pathogen was *staphylococcus aureus*).

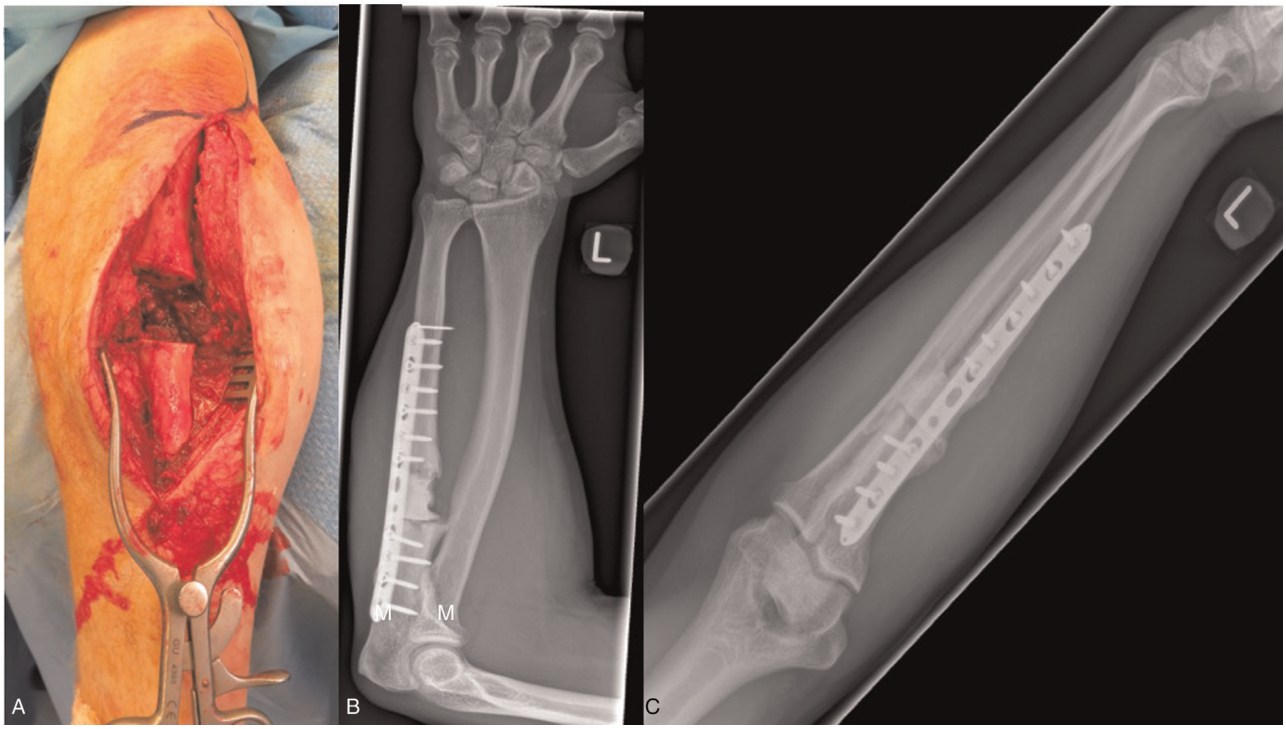

Figure 3. (A) Intraoperative photograph demonstrating the bone defect created following radical debridement of the infected bone edges. (B) AP and (C) lateral postoperative radiographs demonstrating reconstruction of ulna and cement spacer in the area of the defect (first-stage Masquelet technique).

et al[17] have analyzed 40 consecutive fractures (with 19 open fractures) of the tibia shaft. Despite the fact that open fractures included were without segmental bone loss, this study reported excellent outcomes with no amputations, no mal-unions, and few (4) delayed unions.

Interestingly, one of the problems in analyzing data from the literature is that infected and noninfected cases with critical size bone defects are often presented together making the clear discrimination and analysis of the cases difficult or even impossible. In a narrative review of the literature, Aktuglu

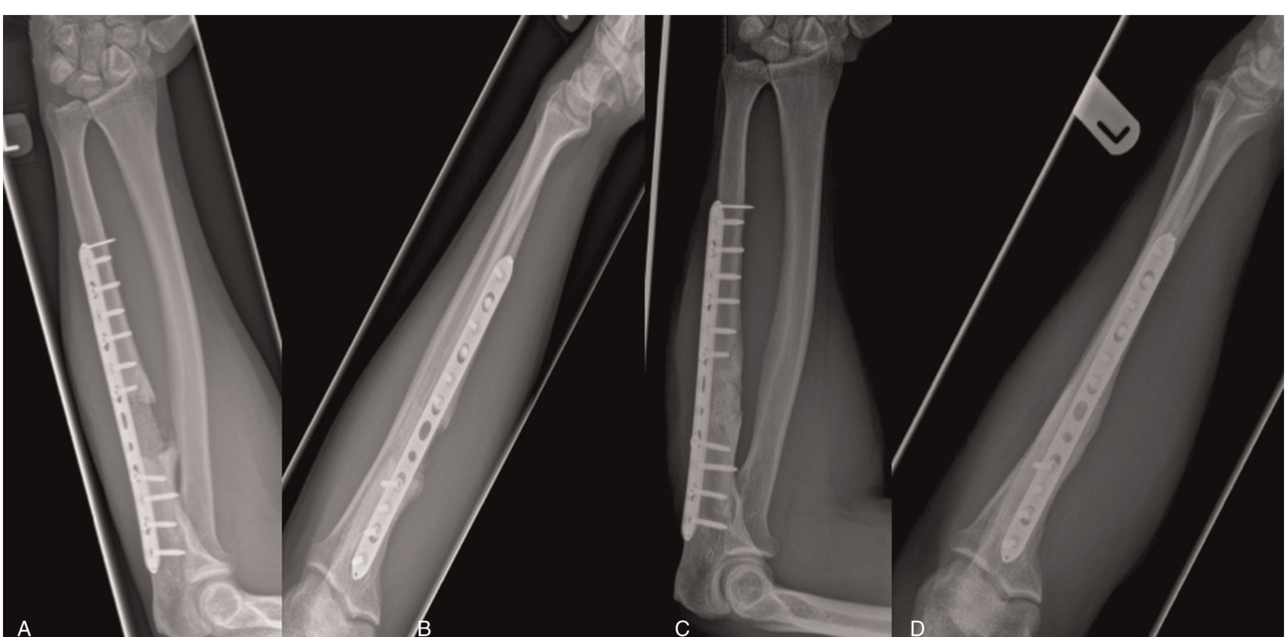

Figure 4. (A) AP and (B) lateral postoperative radiographs after second stage of Masquelet technique (6 weeks from first stage) demonstrating removal of cement spacer and autologous bone grafting to the defect area. (C) AP and (D) lateral postoperative radiographs 4 months later showing osseous healing of the bone defect area.

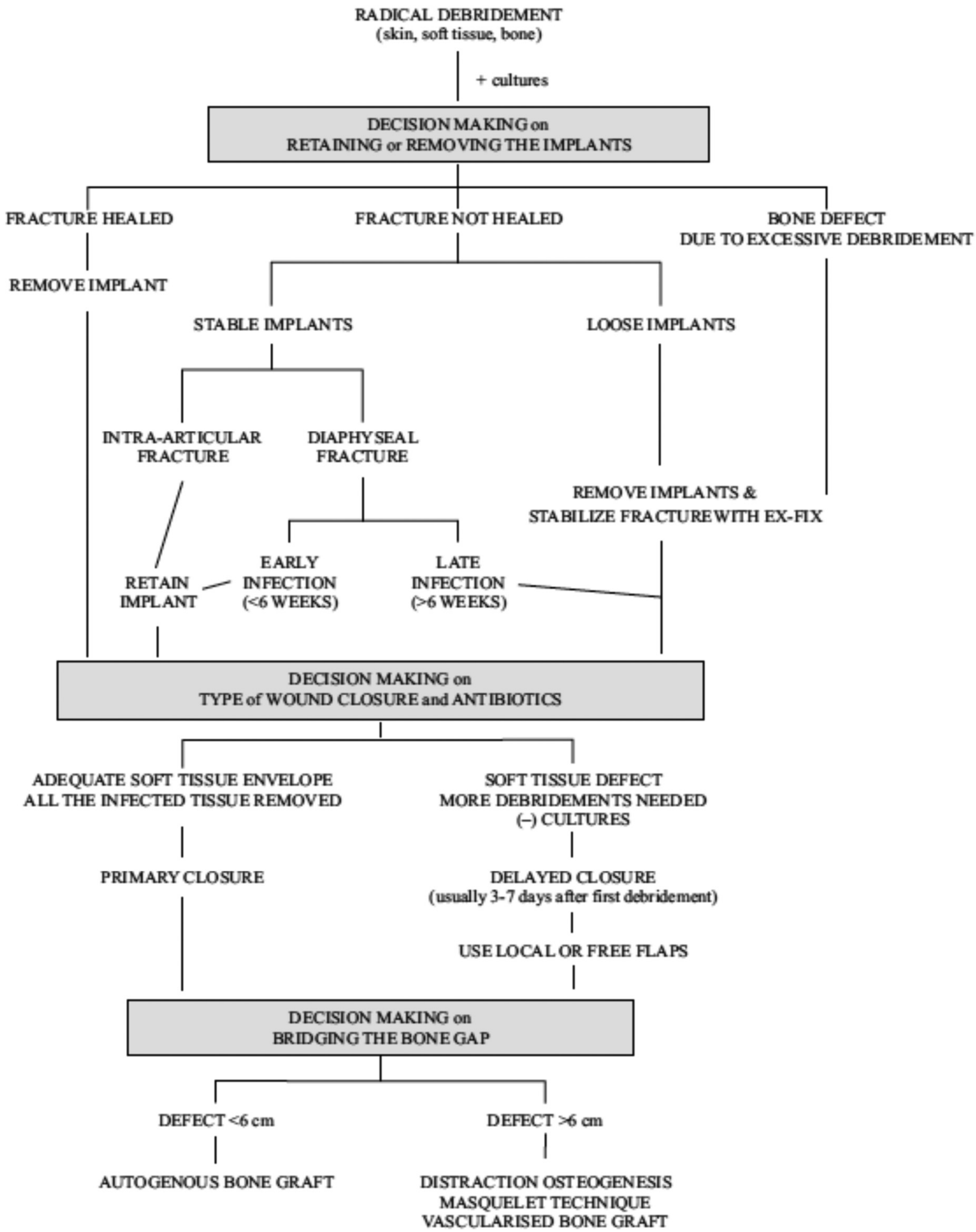

Figure 5. In-house algorithm of management of bone infections.

et al[18] identified 18 studies conducted between 2008 and 2018, which included only infected critical size bone defects of the tibia in their analysis. The authors also identified 6 studies with mixed cases of infected and noninfected tibial cases. Yin et al[19] in a systematic review of the literature using suboptimal/unclear methodology, commented on the infected nonunions of the tibia. The authors included studies from 2004 to 2011 in their study. The mean bone deficit after the debridement of the infected bone was 6.01 ± 1.99 cm (range 3.5–10.7 cm). The study reports bone union rate of 96.69% (range 87%–100%) with low complication rate and mean external fixation time of 9.19 ± 2.22 months (range 3.1–13.9 months).

Two additional systematic reviews [20,21] took into consideration femoral and tibial nonunions. Papakostidis et al[20] using robust methodology reported on 37 studies with a total of 898 patients with femoral and tibial nonunions that were treated with Ilizarov technique from 1989 to 2012. All but 3 studies included infected cases. In tibial defects without discriminating the infected from the noninfected cases, the authors reported 3.7 times increase in the odds of refracture when the size of the tibial defect exceeded 8 cm. This was the only correlation that was made between the size of the defect and other parameters/outcomes of this study. In a systematic review and meta-analysis Yin et al[21] evaluated the use of the Ilizarov method in the treatment of infected nonunions of the tibia and the femur. To the best of our knowledge this is the only review exclusively dealing with infected cases that resulted in a significant bone loss after the surgical debridement and were managed with the Ilizarov method. The review included 24 studies and 590 patients. The mean age of all patients was 22.7 years and as expected many of them had multiple procedures in the past, that is, 3.64 previous surgical procedures. The mean bone defect was 6.70 cm. The patients with a femoral and a tibial nonunion had mean bone defect of 8.05 cm and 6.54 cm respectively. The mean follow-up of the patients included was more than 3 years (39.79 months). The authors reviewed the union rate, the functional results, and complications. They reported an overall union rate of 97.26%. The overall time with the fixation on the bone was 10.69 months. Of note is the fact that the overall time with the fixation on was substantilaly more for the patients with the femoral nonunion (18.26 months) as oppposed to the patients with a tibial nonunion (9.41 months). The authors also reported low complication rates and adverse events (4%, 7%, 5%, 12%, 4%, 13%, and 13% for rate of refracture, malunion, infectious recurrence, knee stiffness, amputation, limb edema, and peroneal nerve palsy respectively) and concluded that the Ilizarov method represents a good method for the treatmenat of infected femoral and tibial nonunions.

2. Conclusion

Acute and chornic infection with both soft tissue and bone involvement remain difficult to manage even in the most experienced surgical hands. Multidisciplinary team involvement is manadatory. Application of a gold standard approach is not possible due to the high heterogeneous patient population and the variable degree of severity of soft tissue and bone involvement. The mainstay of treatment remains the conversion of a septic environment to an aseptic one. Subsequently, reconstruction of the soft tissue defect can be achieved using modern microsurgical techniques (Fig. 5).[22] The induced membrane and distraction osteogenesis are the 2 most commonly used techiques in the management of osteomyelitis and infected nonunions when the surgical debridement results in critical-sized bone defects. Both methods yield good results provided that strick adherence to the basic principles of their technique is followed. The Masquelet method is ever evolving, and outcomes will continue to improve as our knowledge expands on how to optinize all the steps of this technique.

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