[5] Cierny G. Chronic osteomyelitis: results of treatment. Instr Course Lect. 1990;39:495–508.
[6] Cierny G. Infected tibial nonunions (1981-1995). The evolution of change. Clin Orthop Relat Res. 1999:97–105.
[7] Allende C. Cement spacers with antibiotics for the treatment of posttraumatic infected nonunions and bone defects of the upper extremity. Tech Hand Up Extrem Surg. 2010;14:241–247. doi:10.1097/BTH.0b013e3181f42bd3.
[8] Chan Y, Ueng SW, Wang C, Lee S, Chen C. Antibiotic-impregnated autogenic cancellous bone grafting is an effective and safe method for the management of small infected tibial defects: a comparison study. J Trauma. 2000;48:246–255.
[9] 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–e193. doi:10.1097/BOT.0000000000000500.
[10] Green SA, Dlabal TA. The open bone graft for septic nonunion. Clin Orthop Relat Res. 1983:117–124.
[11] Esterhai JJ, Sennett B, Gelb H, Heppenstall R, Brighton C, Osterman A, et al. Treatment of chronic osteomyelitis complicating nonunion and segmental defects of the tibia with open cancellous bone graft, posterolateral bone graft, and soft-tissue transfer. J Trauma. 1990;30:49–54.
[12] Ueng SW, Shih C-H. Semiopen cancellous bone grafting. A 2 step method for closing small infected tibial bone defects. Clin Orthop Relat Res. 1994;306:175–182.
[13] Patzakis M, Scilaris T, Chon J, Holtom P, Sherman R. Results of bone grafting for infected tibial nonunion. Clin Orthop Relat Res. 1995;315:192–198.
[14] Emami A, Mjöberg B, Larsson S. Infected tibial nonunion: good results after open cancellous bone grafting in 37 cases. Acta Orthop. 1995;66:447–451. doi:10.3109/17453679508995585.
[15] Cove JA, Lhowe DW, Jupiter JB, Siliski JM. The management of femoral diaphyseal nonunions. J Orthop Trauma. 1997;11:513–520.
[16] Chen C-Y, Ueng SW-N, Shih C-H. Staged management of infected humeral nonunion. J Trauma Inj Infect Crit Care. 1997;43:793–798.
[17] Ueng SW, Wei -C, Shih CH. Management of femoral diaphyseal infected nonunion with antibiotic beads local therapy, external skeletal fixation, and staged bone grafting. J Trauma Inj Infect Crit Care. 1999;46:97–103.
[18] Tulner SAF, Schaap GR, Strackee SD, Besselaar PP, Luitse JSK, Marti RK. Long-term results of multiple-stage treatment for posttraumatic osteomyelitis of the tibia. J Trauma. 2004;56:633–642. doi:10.1097/01.TA.0000112327.50235.0A.
[19] Chen CE, Ko JY, Pan CC. Results of vancomycin-impregnated cancellous bone grafting for infected tibial nonunion. Arch Orthop Trauma Surg. 2005;125:369–375. doi:10.1007/s00402-005-0794-6.
[20] Jain AK, Sinha S. Infected nonunion of the long bones. Clin Orthop Relat Res. 2005:57–65. doi:10.1097/01.blo.0000152868.29134.92.
[21] Babhulkar SS, Pande K, Babhulkar S. Nonunion of the diaphysis of long bones. Clin Orthop Relat Res. 2005:50–56. doi:10.1097/01.blo.0000152369.99312.c5.
[22] Schöttle PB, Werner CML, Dumont CE. Two-stage reconstruction with free vascularized soft tissue transfer and conventional bone graft for infected nonunions of the tibia: 6 Patients followed for 1.5 to 5 years. Acta Orthop. 2005;76:878–883. doi:10.1080/17453670510045534.
[23] Chiang CC, Su CY, Huang CK, Chen WM, Chen TH, Tzeng YH. Early experience and results of bone graft enriched with autologous platelet gel for recalcitrant nonunions of lower extremity. J Trauma. 2007;63:655–661. doi:10.1097/01.ta.0000219937.51190.37.
[24] Stafford PR, Norris BL. Reamer-irrigator-aspirator bone graft and bi Masquelet technique for segmental bone defect nonunions: a review of 25 cases. Injury. 2010;41:S72–S77. doi:10.1016/S0020-1383(10)70014-0.
[25] Schröter S, Ateschrang A, Flesch I, Stöckle U, Freude T. First mid-term results after cancellous allograft vitalized with autologous bone marrow for infected femoral non-union. Wien Klin Wochenschr. 2016;128:827–836. doi:10.1007/s00508-015-0797-4.
[26] Scholz AO, Gehrmann S, Glombitza M, Kaufmann RA, Bostelmann R, Flohe S, et al. Reconstruction of septic diaphyseal bone defects with the induced membrane technique. Injury. 2015;46:S121–S124. doi:10.1016/S0020-1383(15)30030-9.
[27] Olesen UK, Eckardt H, Bosemark P, Paulsen AW, Dahl B, Hede A. The Masquelet technique of induced membrane for healing of bone defects. A review of 8 cases. Injury. 2015;46:S44–S47. doi:10.1016/S0020-1383(15)30054-1.
[28] El-Alfy BS, Ali AM. Management of segmental skeletal defects by the induced membrane technique. Indian J Orthop. 2015;49:643–648. doi:10.4103/0019-5413.168757.
[29] Canavese F, Corradin M, Khan A, Mansour M, Rousset M, Samba A. Successful treatment of chronic osteomyelitis in children with debridement, antibiotic-laden cement spacer and bone graft substitute. Eur J Orthop Surg Traumatol. 2017;27:221–228. doi:10.1007/s00590-016-1859-7.
[30] Davis JA, Choo A, O'Connor DP, Brinker MR. Treatment of infected forearm nonunions with large complete segmental defects using bulk allograft and intramedullary fixation. J Hand Surg. 2016;41:881–887. doi:10.1016/j.jhsa.2016.05.021.
[31] Giannoudis P V., Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury. 2016;47:S53–S61. doi:10.1016/S0020-1383(16)30840-3.
[32] Pollon T, Reina N, Delclaux S, Bonnevialle P, Mansat P, Bonnevialle N. Persistent non-union of the humeral shaft treated by plating and autologous bone grafting. Int Orthop. 2017;41:367–373. doi:10.1007/s00264-016-3267-3.
[33] Gupta G, Ahmad S, Zahid M, Khan AH, Sherwani MKA, Khan AQ. Management of traumatic tibial diaphyseal bone defect by "induced-membrane technique." Indian J Orthop. 2016;50:290–296. doi:10.4103/0019-5413.181780.
[34] Wang X, Luo F, Huang K, Xie Z. Induced membrane technique for the treatment of bone defects due to post-traumatic osteomyelitis. Bone Joint Res. 2016;5:101–105. doi:10.1302/2046-3758.53.2000487.
[35] Mühlhäusser J, Winkler J, Babst R, Beeres FJP. Infected tibia defect fractures treated with the Masquelet technique. Med U S. 2017;96:1–7. doi:10.1097/MD.0000000000006948.
[36] Ryzewicz M, Morgan SJ, Linford E, Thwing JI, de Resende GVP, Smith WR. Central bone grafting for nonunion of fractures of the tibia: a retrospective series. J Bone Joint Surg Br. 2009;91-B:522–529. doi:10.1302/0301-620X.91B4.21399.

3.5. TREATMENT: MANAGEMENT OF HARDWARE

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QUESTION 1: When should hardware be removed when treating surgical site infection (SSI) in orthopaedic trauma?

RECOMMENDATION: The decision to retain or remove hardware differs by clinical scenario and must take into account extent of the infection and stability of the hardware and fracture.

A methodical approach that addresses the pathogen, host factors and bony and soft tissue deficiencies is required, and includes thorough debridement, dead-space management and soft tissue and bony reconstruction using the established principles of the reconstruction ladder.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 95%, Disagree: 0%, Abstain: 5% (Unanimous, Strongest Consensus)

RATIONALE

Acute or Subacute Infection with Stable Hardware and Fixation

When dealing with orthopaedic implant-related infections, the most common recommendation of nonsurgical consultants is to remove all hardware, obtain deep cultures and administer antibiotics. This is unfortunately only partially correct. Cultures are helpful, and antibiotics are essential, but the removal of stable, functioning hardware in the setting of an acutely infected fracture should generally be resisted. Although it is well-known that the presence of inanimate material surfaces increases the risk of infection, lowers the inoculum necessary to cause infection and reduces the chances of successful treatment, longstanding clinical experience has demonstrated that skeletal stability reduces the infection rate [2,3]. This reduction is supported by the results of animal studies [4,5]. The mechanism by which instability promotes infection is not clear, but may have to do with interference with revascularization of injured tissues, ongoing tissue damage, altered fluid-flow behavior locally or increased micro-dead space. Although instability seems to interfere with the resolution of infection, the presence of infection does not necessarily prohibit bone healing. A logical strategy is to maintain stable internal fixation, which will facilitate union, and plan for hardware removal later if infection persists after the bone is healed.

For the treatment of acutely infected fractures, Berkes et al. reported a 72% rate of fracture union and resolution of infection utilizing a standardized protocol of operative debridement, retention of *stable* fracture hardware and culture-specific intravenous antibiotics. Factors that were predictors of treatment failure included the injury being an open fracture ($p = 0.03$), the presence of an intramedullary nail ($p = 0.01$), a high association with smoking and any infection with Pseudomonas species or other gram-negative organisms [6].

Other authors have also identified factors that contribute to the successful salvage of acutely infected fractures. These include the maintenance of stable hardware and time of surgery to infection diagnosis less than two weeks [7].

Another factor for successful salvage is the ability to achieve a thorough debridement of the fracture construct. If a collection of pus exists around an implant or under a flap or incision, it must be thoroughly drained. Incisions made for irrigation and debridement of infection should rarely be closed and should be placed carefully to avoid exposing hardware, bone, tendon or neurovascular structures. If these are unavoidably exposed, consideration should be given to flap coverage of the wound. The ability to achieve competent wound closure is another predictor of successful salvage. Vacuum-assisted closure (VAC, (Kinetic Concepts, Inc.)) dressing can be used temporarily in the short-term while awaiting definitive coverage.

As mentioned previously, culture specific antibiotic treatment should be standard when treating acutely infected stably fixed fractures. Furthermore, consideration to adding rifampin to culture proven Staphylococcal infections should be strongly considered. A randomized controlled trial to evaluate the utility of adding rifampin to Staphylococcal infection associated with stable orthopaedic implants demonstrated a 100% cure rate in the group treated with ciprofloxacin-rifampin compared to the 58% cure rate in the group receiving ciprofloxacin-placebo [8]. All patients underwent an initial debridement followed by a two-week course of an intravenous antibiotic regimen of flucloxacillin or vancomycin with rifampin or placebo. Long-term therapy was either ciprofloxacin-rifampin or ciprofloxacin-placebo.

In a study by Rightmire, et al. [9] outcomes in patients with acute infections after fracture repair managed with retained hardware were reviewed. They evaluated the effectiveness of irrigation, debridement and antibiotic suppression in the setting of retained hardware. A successful outcome was defined as a patient obtaining fracture union with the original hardware in place. A failure was defined as a patient requiring hardware removal before fracture union [9]. There was only 68% success with an average of 120 days until fracture healing, and 36% of these patients went on to present with reinfection. The majority of the infected fractures that failed debridement and antibiotics with retained hardware failed within three months.

It is important to consider all information when deciding to retain or remove hardware in treatment of these infections, including the specific characteristics of the fracture, the type of fixation, the virulence of the pathogen and physiology and function of the patient.

Acute or Subacute Infection with Unstable Fracture, Fixation and/or Hardware

The presence of excessive motion, the displacement of hardware on radiographs or the visualization of radiolucencies around screws, rods or fixator pins denotes an unstable situation. This instability compromises the ability to overcome infection and to heal the fracture. Bacteria that are attached to surfaces such as metallic fixation devices or dead bone become resistant to the action of antibiotics through the production of biofilm. In the face of unstable hardware or fracture malalignment, the hardware should be removed.

Animal studies with an infected fracture model document the detrimental effects of fracture instability. The infection rates at two weeks post-infection were lower in internally-fixed fractures with stable fixation compared to unstable fractures with loose pins. Stability lowers the incidence of *S. aureus* infection and other gram-positive organisms. However, gram-negative infections were less likely to be successfully suppressed in the internally fixed group and the infection could only be eradicated if the hardware was removed [5].

Friedrich et al. noted similar findings in infected fractures with retained hardware [4] and infection developed in 45% of unstable fractures. However, infection did NOT occur after rigid fixation. With rigid fixation, no significant difference in the time to bony union was noted between the infected versus uninfected fractures. It is important to note that fracture instability, particularly with loss of fixation, may also be a confounded clinical scenario, demonstrating a more widespread infection that prevents callus formation and leads to bone loss and loss of fixation.

Chronic Osteomyelitis

Debridement

Chronic infection after injury is largely a surgical disease and is rarely successfully treated by antibiotics alone. Surgical debridement should be undertaken by experienced surgeons using particular techniques that adhere to established principles, many originally described by Cierny [10–14]. If infection persists after fracture union, hardware must be removed and avascular bone and soft tissue debrided. In general, previous incisions should be used, and all necrotic soft tissue should be removed [10–14]. In the case of structures important to function and with questionable viability (tendons and ligaments), a staged approach can be taken. Care should be taken to not strip viable periosteum from bone. Sclerotic or sequestered bone should be removed until all the remaining bone appears healthy and bleeds well. A high-speed burr is a gentle way to accomplish removal of necrotic infected bone [10–14].

Local Antibiotic Delivery

To prepare defects for grafting or coverage following debridement, antibiotic-impregnated polymethyl methacrylate (PMMA) beads, rods or blocks are often placed to deliver a high concentration of antibiotics locally while avoiding systemic toxicity. Antibiotic elutes from the PMMA by diffusion from the surface. Although most of the drug elutes in the first 24 hours, therapeutic levels of drugs have been detected in some cases for as long as 90 days. Tissue concentrations may be higher and persist longer than those seen in elution experiments. Although many surgeons believe that antibiotic beads used to treat osteomyelitis should be removed, one retrospective study suggested that improved outcomes followed leaving the beads in situ [14].

After removal of an intramedullary rod, placement of antibiotic beads offers no mechanical support. Beads within the intramedullary canal must be removed within 10 to 14 days or subsequent removal may be extremely difficult [15,16]. Antibiotic cement rods can be custom-made at the time of surgery using varying chest tubes as molds [16]. Following thorough medullary canal debridement, the antibiotic rod is inserted and does provide some mechanical stability. If additional debridements are necessary, the antibiotic rod is exchanged. At the time of definitive closure, the antibiotic rod is left intact in the canal, and the wound is closed directly over it. After a six- to eight-week interval, the rod can be removed and bony reconstruction can be undertaken.

REFERENCES

[1] Lowenberg DW, Watson JT, Levin LS. Advances in the understanding and treatment of musculoskeletal infections. Instr Course Lect. 2015;64:37–49.
[2] Strauss EJ, Petrucelli G, Bong M, Koval KJ, Egol KA. Blisters associated with lower-extremity fracture: results of a prospective treatment protocol. J Orthop Trauma. 2006;20:618–622. doi:10.1097/01.bot.0000249420.30736.91.
[3] Mader J, Cripps M, Calhoun J. Adult posttraumatic osteomyelitis of the tibia. Clin Orthop Relat Res. 1999;360:14–21.
[4] Friedrich B, Klaue P. Mechanical stability and post traumatic osteitis: an experimental evaluation of the relation between infection of bone and internal fixation. Injury. 1977;9:23–29.
[5] Merritt K, Dowd JD. Role of internal fixation in infection of open fractures: studies with Staphylococcus aureus and Proteus mirabilis. J Orthop Res. 1987;5:23–28. doi:10.1002/jor.1100050105.
[6] Berkes M, Obremskey WT, Scannell B, Ellington JK, Hymes RA, Bosse M. Maintenance of hardware after early postoperative infection following fracture internal fixation. J Bone Joint Surg Ser A. 2010;92:823–828. doi:10.2106/JBJS.I.00470.
[7] Steve WNU, Wei FC, Sliih CH. Management of femoral diaphyseal infected nonunion with antibiotic beads local therapy, external skeletal fixation, and staged bone grafting. J. Trauma. 1999;97–103. doi:10.1097/00005373-199901000-00016.
[8] Zimmerli W, Widmer AF BM. Role of Rifampin for treatment of orthopedic implant – related Staphylococcal infections a randomized controlled trial. JAMA. 1998;279:1537–1541.
[9] Rightmire E, Zurakowski D, Vrahas M. Acute infections after fracture repair: management with hardware in place. Clin Orthop Relat Res. 2008;466:466–472. doi:10.1007/s11999-007-0053-y.
[10] Tetsworth K, Cierny G. Osteomyelitis debridement techniques. Clin Orthop Relat Res. 1999:87–96.
[11] Heitmann C, Patzakis MJ, Tetsworth KD, Levin LS. Musculoskeletal sepsis: principles of treatment. Instr Course Lect. 2003; 52:733–743.
[12] Cierny G. Chronic osteomyelitis: results of treatment. Instr Course Lect. 1990;39:495–508.
[13] Cierny G. Infected tibial nonunions (1981-1995). The evolution of change. Clin Orthop Relat Res. 1999:97–105.
[14] Henry SL, Hood G a, Seligson D. Long-term implantation of gentamicin-polymethylmethacrylate antibiotic beads. Clin Orthop Relat Res. 1993:47–53.
[15] Patzakis M. Management of acute and chronic osteomyelitis. Oper Orthop. 1993: 3533–3560.
[16] Paley D, Herzenberg JE. Intramedullary infections treated with antibiotic cement rods: preliminary results in nine cases. J Orthop Trauma. 2002;16:723–729. doi:10.1097/00005131-200211000-00007.

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QUESTION 2: Which surgical treatment (plate, nail or external fixator) for open tibial shaft fractures results in lower rate of infection?

RECOMMENDATION: There is little to no difference in terms of infection rates for Gustilo-Anderson types I–II treated by either circular external fixator, unreamed intramedullary nail or reamed intramedullary nail. For Gustilo-Anderson IIIA-B fractures, circular external fixation appears to provide the lowest infection rates when compared to all other fixation methods.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A systematic review was undertaken on all English language articles on infection rates following the treatment of open tibial shaft fractures. The literature search included Google Scholar and the Medline, Embase and Cochrane databases. The search terms included open tibia, tibia fracture and tibial diaphysis with the Boolean terms 'AND' and 'OR.' All abstracts were reviewed, and the full articles were obtained for all potentially suitable articles.

Review articles and those that included peri-articular open fractures and pediatric fractures were excluded. A total of 54 articles were excluded for review. Information regarding Gustilo-Anderson types and infection rates were extracted from all included articles (Table 1).

Statistical analysis revealed that across all Gustilo-Anderson types, circular external fixation and intramedullary nailing have significantly lower infection rates compared to plate fixation or monolateral external fixation. Across all types, there is minimal to no difference between circular external fixation and unreamed intramedullary nailing or reamed intramedullary nailing (Table 2).

When Gustilo-Anderson type IIIB injuries are isolated, circular external fixation appears to have a significantly lower risk of risk of infection when compared to reamed and undreamed intramedullary nail fixation (Table 4).

In conclusion, from the available published English literature on infections rates for open tibial shaft fractures treated by various different fixation methods, plate fixation and monolateral external fixation have significantly higher infection rates when compared to circular external fixation or intramedullary nailing. There appears to be little to no difference for Gustilo-Anderson types I – IIIA treated by either circular external fixator, unreamed intramedullary nail or reamed intramedullary nail. For Gustilo-Anderson type IIIB fractures, circular external fixation appears to provide the lowest infection rates when compared to all other fixation methods.

REFERENCES

[1] Gopal S, Majumder S, Batchelor AG, Knight SL, De Boer P, Smith RM. Fix and flap: the radical orthopaedic and plastic treatment of severe open fractures of the tibia. J Bone Joint Surg Br. 2000;82:959–966.
[2] Clifford RP, Beauchamp CG, Kellam JF, Webb JK, Tile M. Plate fixation of open fractures of the tibia. J Bone Joint Surg Br. 1988;70:644–648.
[3] Bach AW, Hansen ST. Plates versus external fixation in severe open tibial shaft fractures. A randomized trial. Clin Orthop Relat Res. 1989:89–94.