Title
Critical-Sized Bone Defects: Sequence and Planning.

Journal
Journal of orthopaedic trauma, 31 Suppl 5(Suppl 5)

ISSN
0890-5339

Authors
Toogood, Paul
Miclau, Theodore

Publication Date
2017-10-01

DOI
10.1097/bot.0000000000000980

Peer reviewed

Critical-sized bone defects: Sequence and planning

Paul Toogood, MD*, Theodore Miclau, MD

Department of Orthopaedic Surgery, University of California, San Francisco, UCSF/ZSFG Orthopedic Trauma Institute, 2550 23rd St. Building 9, 2nd floor, San Francisco CA 94110

* Corresponding author: Paul.toogood@ucsf.edu, phone 415-206-8812, fax 415-206-3733.

Conflict of Interest Statement: Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Funding Statement: No funding source was used to produce this manuscript.

Abstract

Bone defects associated with open fractures require a careful approach and planning. At initial presentation, an emergent irrigation and debridement is required. Immediate definitive fixation is frequently safe, with the exception of those injuries that normally require staged management or very severe type IIIB and IIIC injuries. Traumatic wounds that can be approximated primarily should be closed at the time of initial presentation. Wounds that cannot be closed should have a negative pressure wound therapy dressing applied. The need for subsequent debridements remains a clinical judgement, but all non-viable tissue should be removed prior to definitive coverage. Cefazolin remains the standard of care for all open fractures, and type III injuries also require gram-negative coverage. Both the induced membrane technique (IMT) with staged bone grafting and distraction ostogenesis (DO) are excellent options for bony reconstruction. Soft tissue coverage within one week of injury appears critical.

Introduction:

Large bone defects caused by traumatic open fractures are complex and can overwhelm both the patient and the surgeon who together must make a large series of decisions on a lengthy reconstructive pathway. The purpose of this article is to review the sequence of decision-making for these difficult injuries. Specifically, this article will address: 1) Initial debridement; 2) Subsequent debridements and medical management; and 3) Definitive reconstruction.

Key Words: Bone defect, soft tissue management, trauma

Initial Debridement:

<u>Management of the bony injury:</u>

How much to debride?

Although open fractures are common and frequently studied, it remains true that surgical principles, rather than evidence based medicine, continues to guide open fracture debridement. Even contemporary investigations simply state that open fractures should be debrided until "stable" and "all necrotic tissue and organic and inorganic contaminants have been removed".[1] Unfortunately quantifying debridement beyond these subjective descriptions remains illusive.

A frequent, specific scenario relevant to the topic of critical-sized bone defects is the large bone fragment that remains in the wound and is devoid of soft tissue attachments. While retaining this fragment may risk infection and has led authors to recommend radical debridement,[2] removing such a fragment undoubtedly worsens the reconstructive challenge. The decision of whether to retain or remove a major bony fragment requires weighing the risks and benefits.

The surgeon must first determine the value of the specific bone fragment. On one end of the spectrum, there is the low value fragment, such as a moderate sized diaphyseal fragment, which can be managed easily with contemporary techniques. At the other extreme is the high value fragment, such as a large osteochondral fragment or whole extruded bone that is essentially irreplaceable.

When considering the low value diaphyseal fragment, the current practice is to remove this fragment.[3] While direct comparisons of retention versus debridement of such fragments is lacking, it is generally accepted that devascularized fragments can serve as a nidus for infection. Although removal of such fragments often requires later procedures to achieve union, excision appears to be a justifiable step, as the treatment of a critical-sized defect is preferable to the management of established osteomyelitis.

The same cannot be said for large osteochondral fragments. Large sections of articular surface, once removed, allow for limited reconstructive options: allograft replacement, primary arthroplasty, or joint fusion. In such a scenario, cleaning and retaining such a fragment becomes a reasonable option. An extruded talus represents a dramatic example of such a fragment. Short of re-implantation, there is nothing a surgeon can do to re-establish normal anatomic relationships from this injury, and multiple authors have reported limited success with debridement and retention.[4-14] Other authors also have reported on the successful treatment of open fractures with cleansing and replantation of devitalized bone fragments.[15-17] Thus, for high value, irreplaceable fragments, debridement and re-implantation remains a reasonable option.

External fixation or early definitive fixation?

Once the debridement is complete, the bone injury requires some form of stabilization. Outside of the need for damage control orthopedics and certain periarticular fractures, surgeons must decide between immediate definitive fixation and initial external fixation with later staged reconstruction. Immediate definitive fixation is attractive as it eliminates the need for subsequent staged internal fixation. The primary argument for external fixation is it avoids the placement of definitive implants in a potentially contaminated wound beds.

Brumback et al. evaluated the treatment of open femur fractures using immediate definitive hardware placement, specifically an intramedullary nail.[18] In this series, none of the 62 type I, II, or IIIA injuries were complicated by infection. Results did worsen for IIIB injuries, where 3 of 27 patients developed an infection.

Tornetta et al. compared immediate intramedullary nailing to definitive external fixation for 29 type IIIB tibia fractures.[19] All patients went on to union and one in each group experienced a deep infection. Similarly, Henley et al. evaluated the treatment of 174 type II, IIIA, and IIIB open tibia fractures treated with immediate intramedullary nail or definitive external fixation.[20] While more severe injuries predicted higher infection and nonunion rates, the choice of an immediate intramedullary nail did not appear to significantly increase infection rates. Both reports noted the relative ease of caring for patients with internal fixation versus external fixation. While neither report directly compared immediate definitive fixation to external fixation and staged definitive fixation, higher rates of infection were not seen with initial definitive fixation in these series, suggesting that immediate internal fixation following a thorough irrigation and debridement may be reasonable.

In summary, immediate definitive fixation, particularly with an intramedullary device, appears safe and justified in lower grade injuries (types I, II, and IIIA). Infection rates are higher for type IIIB and IIIC injuries and clinical judgment is still necessary in the selection between immediate internal fixation and staged fixation following initial external fixation.[3]

Management of the soft tissue injury:

Should the wound be closed?

Classic surgical principles dictate that infected and traumatic wounds be left open to avoid the containment of sepsis, and indeed open fracture wounds were often left open even if closeable in past decades.[21-24] More recent evidence, however, appears to firmly suggest the benefit of immediate closure for type I, II, and IIIA open fractures. Jenkinson et al., examining 146 patients with open lower extremity fractures, reported an infection rate of 4.1% in wounds that were primarily closed versus 17.8% that underwent delayed closure.[25]

What to apply to a wound that cannot be closed?

When the presenting wounds and their surgical extensions cannot be closed during the initial procedure, the surgeon must then decide how to cover the wound. Most of the early studies of open fractures suggested that such wounds be left completely or partially open after the initial debridement.[21-24] Subsequent studies, however, suggested that allowing nosocomial infections into open wounds, rather than containing initial inoculums from the time of injury, may be the greater concern. In a study that examined 21 type IIIB open fractures that became infected, 57% of local sepsis was caused by organisms not present in the wounds during the first two weeks of treatment.[26] Traditional “wet-to-dry” dressings have given way to negative pressure wound therapy (NPWT). Multiple authors have now shown a dramatic reduction in infection rates with the use of NPWT (5-8%) compared with gauze dressings (~28%).[27, 28] Similarly, other authors have shown both a reduction in gram-negative infection rates[29] and polymicrobial infections with NPWT[30].

Subsequent debridements and medical management:

Are more debridements necessary? When is the wound clean?

Despite major advances in the care of severe lower extremity trauma in the last several decades, there is surprisingly little more than clinical judgment to help surgeons decide when a wound is “clean”. Although open wound cultures initially were felt to be useful as a guide for further debridements and appropriate antibiotic selection, these cultures have not been shown to successfully predict later infection or an infecting organism.[31-33] An on-going multi-center study (Bioburden) by the Major Extremity Trauma Research Consortium (METRC) is evaluating the utility of using polymerase chain reaction (PCR) techniques to characterize wound contamination/colonization at the time of wound closure in severe lower extremity injury.[1] This investigation may provide some much needed insight into objectively determining the health of traumatic wounds. Pending these results and further investigation, existing surgical principles still dictate management: All wounds should be debrided to stable, clean appearing margins, which may require multiple returns to the operating room depending on the visual evolution of the wound over time.

How are antibiotics managed from initial presentation to definitive fixation?

Prompt administration of antibiotics in open fracture management has been shown to have clear benefit. Early publications from Patzakis, Gustillo, and Anderson clearly demonstrated the dramatic reduction in infection rates with the use of antibiotics and the necessity for gram-negative coverage in type III open fractures.[23, 34, 35] Since that time, investigators have emphasized the importance of administering antibiotics early after injury. Infection rates have been shown to rise from 7% to 28% in those patients who received antibiotics within 60 minutes compared to those who received antibiotics 90 minutes or later following injury.[36]

The specifics of which antibiotics to use is less clear. Traditionally, a first generation cephalosporin has been recommended for type I and II open fractures and gentamicin has been added to type III injuries.[23, 35] With the aim of avoiding some of the complications of aminoglycocides, more recent studies have explored the use of alternative gram-negative coverage. Ceftriaxone[37], piperacillin/tazobactam[38], cefotaxime[39], and cefepime[40] have all been investigated and been found to be either superior or no less effective. The addition of penicillin for fecal or potential clostridial contamination is also recommended.[41]

A final consideration is the duration of antibiotics and their relationship to closure or coverage of any open wounds. Current Eastern Association for the Surgery of Trauma (EAST) Guidelines (Luchette, Hoff) recommend the administration of antibiotics for 24 hours after the treatment of type I and II fractures[42, 43] This suggestion is supported by work that demonstrates no difference in infection rates between 1 and 5 days of antibiotic coverage.[44] For type III open injuries, EAST recommends extending coverage for up to 72 hours or 24 hours after definitive closure or coverage.[42, 43]

Definitive Reconstruction:

Management of the bone injury:

Induced membranes technique versus bone transport?

The primary contemporary means of reconstructing critical bone defects are the induced membranes technique, pioneered by Masquelet, and distraction osteogenesis, introduced by Ilizarov. IMT places a cement spacer in a defect, allows the formation of a membrane around it over the course of 6 weeks, and then requires a secondary surgery to remove the spacer and place autograft into the membrane-surrounded defect. DO generates new bone away from a defect at the site of a remote corticotomy; the bone fragment between the corticotomy and the original critical defect is moved slowly to simultaneously narrow the critical defect and generate new bone in the growing corticotomy site.

The results of both IMT and DO are well summarized in recent meta-analyses. Morelli at al. analyzed 17 studies (427 patients) looking at the results of IMT.[45] The mean size of the defects in this review was 5.5cm, with 21% being > 10cm. Complication rates were near 50%, with new infection (~10%), persistent infection or non-union (18%), and the need for further surgery (~36%) all being common. Despite this, the ultimate union rate at 15 months reached almost 90%.

Papakostidis similarly analyzed the results of DO, citing 37 manuscripts (898 patients) with patients with a mean defect between 3.5-11.1cm.[46] Complications were again common with infection ranging from 0-60% for tibias and 0-6.2% for femurs, and re-fracture ranging from 0-19% in tibias and 3.3-7.7% in femurs. However, like IMT, eventual union rates were high, with rates of 94% in tibias and 96% in femurs.

No direct comparisons of IMT and DO exist to suggest which is preferable in a particular patient. Given the heterogeneity of patients and these injuries, it is unlikely that one approach is truly superior to the other. Relatively small defects, defects that are not circumferential, and defects that exist in the presence of stable internal fixation may be better managed with IMT. In contrast, a large bone defect also associated with existing or prior infection or soft tissue loss might be better managed with DO. The need for exceptional patient compliance with fixator lengthening and hygiene, however, may make DO a less attractive option in some patients.

Management of the soft tissue injury:

Timing of soft tissue coverage?

Multiple prior authors have attempted to determine if a correlation exists between the timing of definitive flap coverage and patient outcomes. The Lower Extremity Assessment Project (LEAP) group, in two separate publications, failed to demonstrate timing of flap coverage as an influence on complications rates.[47,48] These authors used 72 hours as the distinction between early and late coverage. Later authors, using a single institution database and 7 days as the inflection point, were able to demonstrate the influence of timing on the rates of flap complications.[49] While no difference in complication rates was noted for days 1-7, each day after 7 days resulted in an 11% increase rate of complications, and 16% increased risk of infection specifically. As such, current evidence appears to suggest an aggressive approach for coverage of 3B open wounds.

References:

1) Bosse MJ, Murray CK, Carlini AR, et al. Assessment of Severe Extremity Wound Bioburden at the Time of Definitive Wound Closure or Coverage: Correlation With Subsequent Postclosure Deep Wound Infection (Bioburden Study). J Orthop Trauma 2017;31:S3–S9.

2) Yaremchuk MJ. Acute management of severe soft-tissue damage accompanying open fractures of the lower extremity. Clin Plast Surg. 1986 Oct;13(4):621-32.

3) Zalavras CG, Patzakis MJ, Open Fractures: Evaluation and Management. J Am Acad Orthop Surg 2003;11:212-219.

4) Mohammad HR, A'Court J, Pillai A. Extruded talus treated with reimplantation and primary tibiotalocalcaneal arthrodesis. Ann R Coll Surg Engl. 2017 Apr;99(4):e115-e117.

5) Lee HS[1], Chung HW[2], Suh JS[3]. Total talar extrusion without soft tissue attachments. Clin Orthop Surg. 2014 Jun;6(2):236-41.

6) Breccia M, Peruzzi M, Cerbarano L, Galli M. Treatment and outcome of open dislocation of the ankle with complete talar extrusion: a case report. Foot (Edinb). 2014 Jun;24(2):89-93.

7) Dumbre Patil SS[1], Abane SR[2], Dumbre Patil VS[2], Nande PN[2]. Open fracture dislocation of the talus with total extrusion: a case report. Foot Ankle Spec. 2014 Oct;7(5):427-31.

8) Gerken N[1], Yalamanchili R, Yalamanchili S, Penagaluru P, Md EM, Cox G. Talar revascularization after a complete talar extrusion. J Orthop Trauma. 2011 Nov;25(11):e107-10.

9) Burston JL, Brankov B, Zellweger R. Reimplantation of a completely extruded talus 8 days following injury: a case report. J Foot Ankle Surg. 2011 Jan-Feb;50(1):104-7.

10) Apostle KL, Umran T, Penner MJ. Reimplantation of a totally extruded talus: a case report. J Bone Joint Surg Am. 2010 Jul 7;92(7):1661-5

11) Mnif H, Zrig M, Koubaa M, Jawahdou R, Hammouda I, Abid A. Reimplantation of a totally extruded talus: a case report. J Foot Ankle Surg. 2010 Mar-Apr;49(2):172-5.

12) Fleming J, Hurley KK. Total talar extrusion: a case report. J Foot Ankle Surg. 2009 Nov-Dec;48(6):690.e19-23.

13) Smith CS, Nork SE, Sangeorzan BJ. The extruded talus: results of reimplantation.
J Bone Joint Surg Am. 2006 Nov;88(11):2418-24.

14) Brewster NT, Maffulli N. Reimplantation of the totally extruded talus. J Orthop Trauma. 1997 Jan;11(1):42-5.

15) Kao JT, Comstock C. Reimplantation of a contaminated and devitalized bone fragment after autoclaving in an open fracture. J Orthop Trauma. 1995;9(4):336-40.

16) Abell CF. Extrusion of femoral shaft by trauma and successful replacement. J Bone Joint Surg 48A: 537-41, 1966.

17) Kirkup JR. Traumatic femoral bone loss. J Bone Joint Surg 47B: 106-110, 1965.

18) Brumback RJ, Ellison PS Jr, Poka A, Lakatos R, Bathon GH, Burgess AR: In- tramedullary nailing of open fractures of the femoral shaft. J Bone Joint Surg Am 1989;71:1324-1331.

19) Tornetta P III, Bergman M, Watnik N, Berkowitz G, Steuer J: Treatment of grade- IIIb open tibial fractures: A prospective

randomised comparison of external fix- ation and non-reamed locked nailing. J Bone Joint Surg Br 1994;76:13-19.

20) Henley MB, Chapman JR, Agel J, Har- vey EJ, Whorton AM, Swiontkowski MF: Treatment of type II, IIIA, and IIIB open fractures of the tibial shaft: A pro- spective comparison of unreamed in- terlocking intramedullary nails and half-pin external fixators. J Orthop Trauma 1998;12:1-7.

21) Patzakis MJ, Wilkins J, Moore TM. Use of antibiotics in open tibial fractures. Clin Orthop Relat Res 1983;(178):31–5.

22) Benson DR, Riggins RS, Lawrence RM, et al. Treatment of open fractures: a prospective study. J Trauma 1983;23:25–30.

23) Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984;24:742–6.

24) Templeman DC, Gulli B, Tsukayama DT, et al. Update on the management of open fractures of the tibial shaft. Clin Orthop Relat Res 1998;(350): 18–25.

25) Jenkinson RJ, Kiss A, Johnson S, et al. Delayed wound closure increases deep-infection rate associated with lower-grade open fractures: a propensity-matched cohort study. J Bone Joint Surg Am 2014;96:380–6.

26) Fischer MD, Gustilo RB, Varecka TF. The timing of flap coverage, bone-grafting, and intramedullary nailing in patients who have a

fracture of the tibial shaft with extensive soft-tissue injury. J Bone Joint Surg Am 1991;73:1316–22.

27) Stannard JP, Volgas DA, Stewart R, et al. Negative pressure wound therapy after severe high open fractures: a prospective randomized study. J Orthop Trauma 2009;23:552–7.

28) Blum ML, Esser M, Richardson M, et al. Negative pressure wound therapy reduces deep infection rate in open tibial fractures. J Orthop Trauma 2012;26:499–505.

29) Moues CM, Vos MC, van den Bemd GJ, et al. Bacterial load in relation to vacuum-assisted closure wound therapy: a prospective randomized trial. Wound Repair Regen 2004;12:11–7.

30) Dedmond BT, Korteis B, Punger K, et al. The use of negative-pressure wound therapy (NPWT) in the temporary treatment of soft-tissue injuries associated with high-energy open tibial shaft fractures. J Orthop Trauma 2007;21:11–7.

31) Murray CK, Hsu JR, Solomkin JS, et al. Prevention and management of infections associated with combat-related extremity injuries. J Trauma. 2008;64(3 suppl):S239–S251.

32) Palmer MP, Altman DT, Altman GT, et al. Can we trust intraoperative culture results in nonunions? J Orthop Trauma. 2014;28:384–390.

33) Lee J. Efficacy of cultures in the management of open fractures. Clin Orthop Relat Res. 1997:71–75.

34) M.J. Patzakis, J.P. Harvey, D. Ivier The role of antibiotics in the management of open fractures. J Bone Joint Surg Am, 56 (1974), pp. 532–541

35) R.B. Gustilo, J.T. Anderson. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses J Bone Joint Surg Am, 58A (1976), pp. 453–458.

36) W.D. Lack, M.A. Karunakar, M.R. Angerame, et al. Type III open tibia fractures immediate antibiotic prophylaxis minimizes infection. J Orthop Trauma, 29 (2015), pp. 1–6

37) L. Rodriguez, H.S. Jung, J.A. Goulet, et al. Evidence-based protocol for prophylactic antibiotics in open fractures: improved antibiotic stewardship with no increase in infection rates. J Trauma Acute Care Surg, 77 (2014), pp. 400–408.

38) J. Redfern, S.M. Wasilko, M.E. Groth, et al. Surgical site infections in patients with type-III open fractures: comparing antibiotic prophylaxis with cefazolin plus gentamicin versus pipercillin/tazobactam. J Orthop Trauma, 30 (2016), pp. 415–419

39) K.D. Johnson, L.B. Bone, R. Scheinberg. Severe open tibia fractures: a study protocol. J Orthop Trauma, 2 (1988), pp. 175–178

40) Maxson B, Serrano-Riera R, Bender M, et al. Vancomycin and cefepime antibiotic prophylaxis for open fractures reduces infection rates in grade III open fractures compared to

cefazolin and gentamicin, avoids potential nephrotoxicity, and does not result in antibiotic resistance with MRSA. Read at the annual meeting of the Orthopaedic Trauma Association. San Diego (CA), October 10, 2015.

41) David C. Carver, MD, Sean B. Kuehn, MD, John C. Weinlein, MD Role of Systemic and Local Antibiotics in the Treatment of Open Fractures. Orthop Clin N Am 48 (2017) 137–153.

42) F.A. Luchette, L.B. Bone, C.T. Born, et al. EAST Practice Management Guidelines work group: practice management guidelines for prophylactic antibiotic use in open fractures. Eastern Association for the Surgery of Trauma (2000) Available at: http://www.east.org/tgp/openfrac.pdf Accessed July 31, 2016

43) W.S. Hoff, J.A. Bonadies, R. Cachecho, et al. EAST Practice Management Guidelines work group: update to practice management guidelines for prophylactic antibiotic use in open fractures. Trauma, 70 (2011), pp. 751–754

44) E.P. Dellinger, E.S. Caplan, L.D. Weaver, et al. Duration of preventive antibiotic administration for open extremity fractures. Arch Surg, 123 (1988), pp. 333–338

45) Morelli I,Drago L, George DA, et al. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury, Int. J. Care Injured 47S6 (2016) S68–S76.

46) C. Papakostidis, M. Bhandari,, P. V. Giannoudis. Distraction

osteogenesis in the treatment of long bone defects of the lower limbs EFFECTIVENESS, COMPLICATIONS AND CLINICAL RESULTS; A SYSTEMATIC REVIEW AND META-ANALYSIS Bone Joint J 2013;95-B:1673–80.

47) Pollak AN, McCarthy ML, Burgess AR. Short-term wound complications after application of flaps for coverage of traumatic soft-tissue defects about the tibia: the Lower Extremity Assessment Project (LEAP) Study Group. J Bone Joint Surg Am. 2000;82:1681–1691.

48) Webb LX, Bosse MJ, Castillo RC, et al. Analysis of surgeon-controlled variables in the treatment of limb-threatening type-III open tibial diaphyseal fractures. J Bone Joint Surg Am. 2007;89:923–928.

49) D’Alleyrand JG, Manson TT, Dancy L, et al. Is Time to Flap Coverage of Open Tibial Fractures an Independent Predictor of Flap-Related Complications? J Orthop Trauma 2014;28:288–293.