Acute Management of Open Fractures: An Evidence-Based Review

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abstract

Open fractures are complex injuries associated with high morbidity and mortality. Despite advances made in fracture care and infection prevention, open fractures remain a therapeutic challenge with varying levels of evidence to support some of the most commonly used practices. Additionally, a significant number of studies on this topic have focused on open tibial fractures. A systematic approach to evaluation and management should begin as soon as immediate life-threatening conditions have been stabilized. The Gustilo classification is arguably the most widely used method for characterizing open fractures. A first-generation cephalosporin should be administered as soon as possible. The optimal duration of antibiotics has not been well defined, but they should be continued for 24 hours. There is inconclusive evidence to support either extending the duration or broadening the antibiotic prophylaxis for type Gustilo type III wounds. Urgent surgical irrigation and debridement remains the mainstay of infection eradication, although questions persist regarding the optimal irrigation solution, volume, and delivery pressure. Wound sampling has a poor predictive value in determining subsequent infections. Early wound closure is recommended to minimize the risk of infection and cannot be substituted by negative-pressure wound therapy. Antibiotic-impregnated devices can be important adjuncts to systemic antibiotics in highly contaminated or comminuted injuries. Multiple fixation techniques are available, each having advantages and disadvantages. It is extremely important to maintain a high index of suspicion for compartment syndrome, especially in the setting of high-energy trauma. [*Orthopedics*. 2015; 38(11):e1025-e1033.]

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Open fractures are often the result of high-energy trauma and can lead to significant long-term morbidity and disability.[1] An open fracture is defined as one with an associated break in the skin that is capable of communicating with the fracture and/or its hematoma.[2] This communication with the outside environment can lead to higher rates of infection, malunion, and nonunion if not recognized and treated appropriately.[1,3,4]

Prior to the 1850s, most surgeons treated open fractures with early amputation because sepsis and gangrene were common sequelae.[5] It was not until the turn of the 20th century that aseptic techniques became widely accepted, with much credit going to the work of the English surgeon Joseph Lister.[5] Called the father of aseptic surgery, Lister was the first to recognize the importance of aseptic technique during surgery. In his 1867 Lancet article, "On the Antiseptic Principle in the Practice of Surgery," Lister reported a series of open fractures that he treated with use of carbolic acid spray applied to wounds, instruments, and dressings.[6] Using this technique, he achieved a dramatic drop in mortality rate, from the historic 25% to 50% down to 9% in his series.[5,6]

Today, more than a century later, although open fracture injuries are no longer a cause of increased mortality, they continue to be a source of significant morbidity and disability following trauma. The aim of this review is to critically evaluate the available evidence for acute management of open fractures in both adults and children.

Etiology

Open fractures can result from a variety of injuries. Common direct mechanisms include high-energy trauma, such as motor vehicle accidents, firearms, and falls from a height. Indirect mechanisms include low-energy torsional injuries, such as those sustained during sports and falls from a standing height. The extent of trauma is directly related to the amount of energy imparted through the mechanism of injury.[7,8]

Epidemiology

Crush injuries are the most common cause of open fractures, followed by falls from a standing height and road traffic accidents.[9] Open fractures occur more commonly in males than in females (7:3), with a mean age of 40.8 and 56 years, respectively.[9] Fractures of the finger phalanges are the most common type, accounting for nearly half of all open fractures with an incidence of $14/10^5$ per year in the general population.[9] Fractures of the tibia and distal radius are the second and third most common open fractures, with an incidence of $3.4/10^5$ per year and $2.4/10^5$ per year in the general population, respectively.[9]

Classification

A number of classification schemes have been developed to characterize open fractures, including the Gustilo, Tscherne, and Orthopedic Trauma Association systems. The Gustilo classification is arguably the most widely quoted in the orthopedic literature (**Table 1**). First published in 1976 and modified in 1984,[10,11] this classification system organizes open fractures in order of worsening prognosis according to the mechanism of injury, level of contamination, soft tissue damage, and fracture complexity (**Table 2**). In a follow-up study, Gustilo et al[3] demonstrated that the risk of infection directly correlated with the fracture grade. Despite its wide use and prognostic value, the Gustilo classification system is not without limitations. Kim and Leopold[12] reported on a series of studies that found a limited interobserver reliability, with agreement ranging from 53% to 60%.[13,14] They logically concluded that the size of the injury at the skin surface did not always reflect the true extent of deep soft tissue injury. This realization has led many to state that the true Gustilo classification of an open fracture is best made in the operating room.[12,15-18]

Initial Evaluation

When managing trauma patients, including those with open fractures, the most critical first goal is saving life. Advanced Trauma Life Support (ATLS) protocol should be immediately implemented at the scene or in the emergency room. Orthopedic evaluation and management should begin as soon as immediate life-threatening conditions have been stabilized. Knowing the mechanism of injury is essential to understanding the amount of energy transferred to the patient and extent of environmental contamination. A systematic inspection of each limb is critical; open fractures may be missed if the examining physician does not circumferentially expose the entire extremity. The dimensions, locations, and degree of soft tissue involvement of open wounds should be noted prior to reduction and/or splinting. A complete neurovascular examination should be performed, and, if necessary, vascular studies should be obtained for those injuries with a questionable vascular examination. It is extremely important to maintain a high index of suspicion for compartment syndrome, especially in the setting of high-energy trauma. The incidence of compartment syndrome is directly proportional to the degree of injury as assessed by the Gustilo grade and has been reported to be as high as 9.1% in open tibial fractures.[19] If there is any clinical suspicion of compartment syndrome and the patient is unable to cooperate with examination, compartment pressures should be assessed.

Initial Management

Although there is no evidence to support preliminary debridement and irrigation of open wounds at the bedside, removing immediately accessible contaminants, such as leaves and clothes, may help eliminate sources of infection because these foreign objects can be pushed deep into soft tissue after preliminary fracture reduction. Obtaining photographs of the wound(s) is also helpful to mini-

mize multiple examinations, which can be painful. Following irrigation, wet-to-dry saline dressing should be applied to aid in healing, comfort, and prevention of infection. Chaby et al[20] performed a systematic review of dressings for acute and chronic wounds and found no evidence that any of the modern dressings (ie, hydrofiber and foam dressings) were better than saline gauze. The limb should then be reduced and placed in a well-padded splint. Pulses should be documented before and after reduction.

Table 1

Short Version of the Gustilo Classification System of Open Fractures[a]

Type	Description
I	Wound <1 cm, clean
II	Wound >1 cm, no extensive soft tissue damage
IIIA	Extensive soft tissue damage with adequate coverage
IIIB	Extensive soft tissue damage with inadequate coverage
IIIC	Arterial injury requiring repair

[a]Data from Gustilo and Anderson[10] and Gustilo et al.[11]

Table 2

Expanded Version of the Gustilo Classification System of Open Fractures[a]

	Fracture Type				
Feature	**I**	**II**	**IIIA**	**IIIB**	**IIIC**
Wound size, cm	<1	>1	>1	>1	>1
Energy	Low	Moderate	High	High	High
Contamination	Minimal	Moderate	Severe	Severe	Severe
Deep soft tissue damage	Minimal	Moderate	Severe	Severe	Severe
Fracture comminution	Minimal	Moderate	Severe/ segmental fractures	Severe/ segmental fractures	Severe/ segmental fractures
Periosteal stripping	No	No	Yes	Yes	Yes
Local coverage	Adequate	Adequate	Adequate	Inadequate	Adequate
Neurovascular injury	No	No	No	No	Yes
Infection rate	0%-2%	2%-7%	7%	10%-50%	25%-50%

[a]Data from Gustilo et al,[3] Gustilo and Anderson,[10] and Gustilo et al.[11]

Wound Cultures

Routine wound cultures before surgical debridement were routinely performed prior to the 1980s,[4,10] but the value of this practice has been called into question in recent years. In a retrospective study of 86 lower extremity open fractures in children, Kreder and Armstrong[21] found that the pathogens in infected cases were only identified in 29% of positive pre-debridement and 60% of post-debridement cultures. These findings were consistent in adults, with several prospective and retrospective studies showing that pre-debridement cultures identified the infecting pathogen in only up to 22% of cases.[22,23] As a result, routine wound cultures before surgical debridement are no longer recommended. Similarly, the value of cultures obtained after surgical debridement remains unknown. Lenarz et al[24] investigated the timing of wound closure and risk of deep infection based on post-debridement cultures in 422 open fractures. There was no difference in the rate of deep infection between wounds closed after positive or negative cultures. However, the study was limited by substantial loss to follow-up and the confounding effect of antibiotics because culture-specific antibiotic therapy was routinely continued until uneventful wound healing.

Tetanus Prophylaxis

The tetanus toxoid vaccine and tetanus immune globulin are used to enhance the immune response to *Clostridium tetani,* an anaerobic gram-positive bacillus found in soil. The initial tetanus vaccination series includes 3 separate doses of the tetanus toxoid. A booster, usually given as a tetanus toxoid/diphtheria toxoid (Td) combination,[25] is recommended every 10 years because the circulating antitoxin may fall below the minimal protective level. Although there are no studies evaluating the benefits of tetanus prophylaxis after open fractures, the severity of the disease, along with the minimal morbidity of administration, has made tetanus prophylaxis a routine practice following open fractures. The correct treatment (complete vaccination series, booster, and/or immune globulin) depends on the extent of wound contamination and the patient's tetanus vaccine status. In general, the tetanus vaccine is provided to patients with incomplete/uncertain vaccination history. The booster is provided to those with 10 years or more of vaccination history, except in cases of contaminated wounds if more than 5 years have elapsed since the last tetanus vaccination history. The teta-

nus immune globulin is reserved for highly contaminated wounds with incomplete/uncertain vaccination history. This is a single intramuscular dose of 3000 to 5000 units of tetanus immune globulin that provides immediate immunity.[25]

Antibiotic Prophylaxis

Indication

Gustilo and Anderson[10] found that 70% of open wounds were contaminated with bacteria and argued that the routine use of antibiotics was a therapeutic rather than a prophylactic measure. Similarly, in a prospective, randomized trial of 1104 open fracture in children and adults, Patzakis and Wilkins[26] found a high rate of bacterial contamination in open wounds and demonstrated a significant reduction in infection rate with early administration of antibiotics. The effectiveness of antibiotics in preventing infection after open long bone fractures was established in a recent meta-analysis of Level I and II studies that showed a relative risk reduction of 43% (95% confidence interval, 29%-65%) when administered pre- or intraoperatively.[27] A subgroup analysis did not find a significant benefit for antibiotics in open finger fractures, which make up nearly half of all open fractures.[9] In addition, the current guidelines of the Surgical Infection Society provide a Level I recommendation against the use of prophylactic antibiotics for open fractures resulting from low-velocity civilian gunshot wounds if surgical fixation is not required.[28]

Timing

Patzakis and Wilkins[26] reported an infection rate of 4.7% when antibiotics were administered within 3 hours of injury, compared with 7.4% when the treatment was delayed more than 3 hours, although the statistical significance of this difference was not provided. Currently, there are no Level I or II studies addressing the optimal window for antibiotic therapy. However, from a clinical practice standpoint, defining this window may be futile because prophylaxis implies that the treatment should be provided at the time of exposure before infection develops. Therefore, the administration of antibiotics should be done as soon as possible.[27]

Choice

In 1974, Patzakis et al[4] performed one of the first randomized, placebo-controlled trials that highlighted the role of first-generation cephalosporins in reducing the infection rate following open fractures. Since then, the efficacy of first-generation cephalosporins in open fractures—excluding open finger fractures and those caused by low-velocity firearms—has been confirmed in multiple Level I and II studies.[27] In the United States, cefazolin is the only first-generation cephalosporin available in intravenous form. It is active against most gram-positive cocci, as well as gram-negative rods, such as *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella pneumoniae*.[29]

Extending antibiotic coverage beyond gram-positive organisms for Gustilo type III open fractures has traditionally been common practice[25,30] despite lack of evidence to support it. This recommendation is based on a historic high rate of wound infections caused by gram-negative organisms in type III open fractures, as initially reported by Gustilo et al.[11] The authors recommended a combination of a first-generation cephalosporin and an aminoglycoside, or a third-generation cephalosporin for type III open fractures.[11] Although normal skin flora and *Staphylococcus aureus* are the most commonly isolated microorganisms from open fracture wounds,[3,4,31] hospital-acquired gram-negative rods, such as *Pseudomonas aeruginosa*, can play a significant role in the pathogenesis of infection, especially in times of delayed wound closure, often experienced in type III injuries.[3] Hence, the addition of an aminoglycoside to cefazolin or substitution with a third-generation cephalosporin is thought to provide coverage against potential nosocomial gram-negative bacilli. In a prospective, randomized study comparing the first- and third-generation cephalosporins in types II and III open fractures, Johnson et al[32] found no statistical difference in the rate of infection between the 2 treatment groups.

The addition of penicillin for gas gangrene prophylaxis is another controversial practice. In a randomized, placebo-controlled trial exploring the efficacy of prophylactic antibiotics in open fractures, Patzakis et al[4] noted 2 cases of gas gangrene from a series of 311 open fractures and recommended the routine addition of penicillin for anaerobic coverage. However, these 2 cases of gas gangrene occurred in the placebo group that did not receive antibiotics. A more recent study reported that it is rare for *C perfringens*, the causative microorganism of gas gangrene, to be resistant to the standard prophylactic antibiotic regimen (first-generation cephalosporins) and advocated avoiding adding penicillin even for high-risk injuries.[28]

Table 3 lists the dosages of the most commonly used antibiotics in the treatment of open fractures.[33]

Duration

The optimal duration of antibiotic course has not been well defined. There is currently no evidence that extending antibiotic converge beyond 24 hours, even for type II and III open fractures, decreases infection rates. In a randomized, double-blind trial of 248 patients between 14 and 65 years old, Dellinger et al[34] showed no statistically significant difference in fracture-site infections between patients randomized to receive a 1-day course of a first-generation cephalosporin compared with a 5-day course of either a first- or second-generation cephalosporin.[34] Similarly, Patzakis and Wilkins[26] found that prolonging the duration of antibiotics beyond 3 days provided no additional benefit on the risk of infection. Prolonged

courses of more than 1 antibiotic for more than 24 hours following severe trauma are associated with resistant infections.[35]

Surgical Debridement

Adequate debridement is arguably the most critical step in preventing infection and promoting healing. The goal is to debride all contaminated and nonviable tissue, including skin, subcutaneous fat, muscle, and bone. The wound should be extended longitudinally for proper inspection of the zone of injury. The bone ends should be delivered, the medullary canal cleaned, and all devitalized bone fragments with no soft tissue attachments removed. Edwards et al[36] found that removal of necrotic bone significantly lowered the infection rate in open fractures. Although bone and skin viability are assessed by their capacity to bleed, muscle viability is assessed by the criteria outlined by Artz et al,[37] which consist of the 4 Cs: color, contractility, consistency, and capacity to bleed. Whenever soft tissue viability or adequacy of debridement is questionable, repeat debridement is necessary.

Timing of Surgery

The optimal timing of surgical debridement is debated. Historically, open fractures were treated with emergent debridement within 6 hours of injury, as reported by Gustilo and Anderson[10] in 1976. This was likely influenced by a 1898 report by Paul Leopold Friedrich, who used mold and dust particles to inoculate guinea pig wounds. Friedrich showed that the contaminating microorganisms reached an infective load within 6 to 8 hours after inoculation and theorized that simple wound debridement was ineffective after this time.[38] Although early studies demonstrated a benefit to emergent debridement in type II and III open fractures,[39] many recent studies showed no advantage for the 6-hour rule provided that antibiotic therapy was initiated.[26,40,41] Skaggs et al[40] performed a retrospective multicenter study of 554 open fractures in children with a mean age of 8.8 years. All patients received antibiotic therapy on arrival to the emergency room but had different time intervals between injury and surgical debridement. The rates of acute infection were similar for patients who had surgery within 6 hours after injury compared with those delayed up to 72 hours, regardless of the Gustilo wound type.[40] Similarly, Spencer et al[42] performed a 5-year prospective study looking at the effect of time to surgical debridement on infection risk. One hundred three patients with 115 open long-bone fractures were included. Surgical debridement was performed in less than 6 hours from time of injury in 60% of cases and in more than 6 hours from injury in 40% of cases. Infection rates were 10.1% and 10.8%, respectively, with no statistical difference. They concluded that open fracture injuries might best be treated during normal daytime hours by regular, experienced teams, with no increased infection risk by delaying operative treatment.[42] Recently, a meta-analysis on the effect of timing to operative debridement following open long-bone fractures found no association between higher infection rates and delayed debridement up to 12 hours.[41]

Table 3

Dosages of Some of the Most Commonly Used Antibiotics in the Treatment of Open Fractures[a]

Antibiotic	Dose
Cefazolin (first-generation cephalosporin)	100 mg/kg/d divided into 3 doses every 8 h, maximum 2 g per dose
Gentamicin (aminoglycoside)	5-7.5 mg/kg/d divided into 3 doses every 8 h
Penicillin	150,000 units/kg/d divided into 4 doses given every 6 h, maximum dose of 6 million units per dose
Clindamycin	15-40 mg/kg/d divided into 3 doses every 8 h, maximum dose of 2.7 g/d

[a]*Data from Johnson et al.*[32]

Irrigation Solution

The optimal irrigation solution has not been established because there are limited studies on this topic. Anglen[43] randomized 400 patients with 458 open fractures to receive normal saline with bacitracin or normal saline with castile soap. There was no difference in infection rates between the 2 groups, although there was a higher risk of wound healing complications in the bacitracin group (9.5% vs 4%; *P*=.03). A Cochrane meta-analysis by Fernandez and Griffiths[44] found no difference in infection rates between isotonic saline irrigation and various forms of water (distilled, boiled, or tap) in open fractures. In a review by Crowley et al,[45] the authors recommended normal saline irrigation without additives, citing concerns about toxicity and adverse healing effects.

Delivery Pressure

There is a general belief that high-pressure irrigation methods may damage bone and soft tissue and further drive contaminants deeper between tissue planes. This belief mainly stems from in vitro and animal model studies[46-48] that also found low-pressure pulse lavage (LPPL) or bulb irrigation to be equivalent to high-pressure pulse lavage (HPPL) in decreasing bacterial loads when irrigation was performed within 4 hours from the time of contamination. However, when irrigation was delayed more than 4 hours, LPPL became ineffective in removing adherent bacteria.[48,49] Recently, the FLOW (Fluid

Lavage of Open Wounds) trial has been developed to evaluate the optimal irrigation solution and pressure for open wounds.[50] In this multicenter, reviewer-blinded study, patients with open fractures were randomized to receive either castile soap or normal saline irrigation delivered via HPPL of LPPL. The primary outcome was reoperation rate due to infection, wound-healing problems, and/or nonunion. Although the results of the pilot trial on 111 patients showed a trend favoring the LPPL technique, the difference was not statistically significant.[50]

Irrigation Volume

A 1990 expert opinion by Gustilo et al[3] recommended irrigation with 5 to 10 L of normal saline or distilled water followed by 2 L of bacitracin solution for all open fractures. More than a decade later, the optimal amount of irrigation has never been established. A recent expert opinion by Anglen[51] proposed an irrigation protocol based on the severity of injury fracture, with 3 L for type I fractures, 6 L for type II fractures, and 9 L for type III fractures.

Antibiotic-Impregnated Devices

The role of antibiotic-impregnated devices in reducing infection following open fractures is increasingly coming to light, with several studies showing them to be important adjuncts to systemic antibiotics and in some cases equally effective to parenteral antibiotics. Ostermann et al[52] retrospectively reviewed 1085 consecutive cases of open fractures, of which 240 received only systemic antibiotics and 845 received systemic antibiotics plus local tobramycin-impregnated polymethyl methacrylate (PMMA) beads. The authors found a significant reduction in acute infection rates in type IIIB and C fractures in the PMMA group. The incidence of local osteomyelitis was also significantly lower in types II and IIIB fractures in the PMMA group.

In addition to antibiotic beads or spacers placed at the site of fracture, antiseptic-coated intramedullary nails (IMN) have been described. In a rabbit model of open tibial fractures inoculated with *S aureus*, Darouiche et al[53] showed that the use of IMN coated with a combination of chlorhexidine and chloroxylenol was associated with a nearly seven-fold reduction of device-related osteomyelitis compared with uncoated IMN. A recent meta-analysis investigating the role of local antibiotic administration in open tibial fractures found a decrease in the infection rate for all Gustilo grades, and in particular in type III open fractures.[54]

Fracture Management

Early fracture stabilization reduces pain, facilitates bed transfers and ambulation, prevents further soft tissue injury, and promotes healing. This is particularly important for intra-articular fractures where early joint motion may be advantageous.[3] There are many different treatment options for open fractures depending on hemodynamic status, fracture location and pattern, and extent of soft tissue injury.

External Fixation

External fixation is an effective temporizing measure in polytrauma patients, particularly in cases of soft tissue defects. It can also be used as a definitive treatment with good results. Edwards et al[36] showed a 93% union rate with external fixation at a median follow-up of 9 months in 202 consecutive type III open tibial fractures. Similarly, in a prospective, randomized trial of 29 patients with type IIIB open tibial fractures treated with external fixation or unreamed IMN, Tornetta et al[55] found no difference in time to healing, range of motion, and infection rate between the 2 groups.

Most studies on open fracture fixation in children have focused on tibial fractures. In a systematic review, Baldwin et al[56] noted a significant trend from external fixation to casting for type I and II open fractures, with external fixation more commonly used in types IIIB and IIIC injuries. Similar findings were demonstrated in another systematic review by Gougoulias et al,[57] who noted that 51.7% of pediatric open tibial fractures were treated with closed reduction and casting, 26.9% with external fixation, and 19.5% with internal fixation.

Intramedullary Nailing

Compared with external fixation, IMN provide the advantage of faster time to weight bearing, fewer subsequent procedures,[58] higher level of patient compliance,[55] and lower incidence of malalignment.[58] Historically, open long-bone fractures were treated with unreamed IMN because disruption of the endosteal blood supply by reaming was thought to cause further damage to the traumatized bone's already compromised blood supply, leading to higher rates of nonunion. Recently, evidence supporting the use of unreamed IMN came from the SPRINT (Study to Prospectively evaluate Reamed Intramedullary Nails in patients with Tibial fractures) trial, which was a multicenter, randomized study that compared the rates of reoperation between reamed and unreamed tibial IMN.[59] Although initial results of the SPRINT trial found no difference between the 2 groups in open fractures,[59] later reports revealed an increased risk of reoperation in the reamed group.[60] In contrast, no difference in infection and nonunion rates was found in open femoral fractures treated with reamed or unreamed IMN based on several retrospective studies.[61,62] The issue of reaming is particularly relevant in the polytrauma patient because it is believed to contribute to the second-hit phenomenon. Following a traumatic event (first hit), there is a systemic release of a number of inflammatory mediators. This systemic inflammatory response can be hyperstimulated by an additional insult, such as reamed IMN, thereby increasing the patient's susceptibility to posttraumatic complications, including acute respira-

tory distress syndrome.[63] This concept has become the basis for the decision making between damage control orthopedics vs early definitive care.[63]

Fixation With Plate and Screws

Traditional plating techniques have generally fallen out of favor for open tibial fractures associated with extensive soft tissue loss. When comparing plate fixation with external fixation for type II and III open tibial fractures, Bach and Hansen[64] reported a six-fold increase in the rate of severe osteomyelitis. However, newer, less invasive plating techniques have emerged that may allow plate fixation to be a viable option in open tibial fractures. In a retrospective analysis of 56 extra-articular proximal tibial fractures, Lindvall et al[65] compared rates of union, malunion, malreduction, infection, and hardware removal between patients treated with IMN or percutaneous locked plating (PLP). Open fractures made up 55% (12 of 22) of the IMN group and 35% (12 of 34) of the PLP group. Four (33%) of the 12 open fractures in the IMN group and 4 (33%) of 12 open fractures in the PLP group became infected. In a randomized, prospective study comparing IMN with plates and screws for all tibial shaft fractures, Vallier et al[66] found an increased risk of infection in open fractures (83% of infections in the study); however, the rates of infection, nonunion, and secondary procedures were similar between the 2 groups.

Bone Grafting

Bone grafting can help in fracture repair and reconstruction of skeletal defects.[32] It can be performed at the time of closure for types I and II open fractures but should be delayed until the wound has healed in type III fractures, owing to the extensive periosteal stripping, soft tissue damage, and possible blood flow compromise associated with these severe injuries.[32] Similarly, recombinant human bone morphogenetic protein-2 (rhBMP-2) can also be used at the time of definitive wound closure to accelerate healing. In 2002, Govender et al[67] published the results of the BESTT (BMP-2 Evaluation in Surgery for Tibial Trauma) trial, which evaluated the efficacy and safety of rhBMP-2 in open tibial fractures. This prospective, controlled, single-blinded study followed 421 patients randomized into 3 intervention groups: IMN, IMN plus 6 mg rhBMP-2, or IMN plus 12 mg rhBMP-2. The primary outcome measure was the rate of secondary interventions due to delayed union or nonunion. At 1-year follow-up, the group randomized to receive the 12 mg total rhBMP-2 had a 44% reduction in the rate of secondary interventions and faster fracture healing compared with the control group with no rhBMP-2. Since the BESTT study, rhBMP-2 has been approved by the US Food and Drug Administration for use in the primary treatment of open tibial shaft fractures.

Wound Closure

Delayed wound closure may increase risk of infection with nosocomial gram-negative microorganisms, such as *Pseudomonas species*, *Enterobacter species*, and methicillin-resistant *S aureus*.[3,68] In a double-blind, randomized trial examining open fractures with adequate soft tissue coverage, Benson et al[69] found no increased risk of infection when wound closure was delayed for 5 days in highly contaminated fractures provided patients received antibiotic prophylaxis and surgical debridement. For wounds with extensive tissue loss (type IIIB and IIIC injuries), Gopal et al[70] favored early internal fracture fixation and flap coverage (within 72 hours). Their conclusion was supported by a higher rate of infection when flap coverage was delayed, although they cautioned that this difference was not statistically significant.

Negative-Pressure Wound Therapy

Most wounds associated with type I open fractures will heal by secondary intention or can be closed primarily without an increased risk of infection.[71] However, higher-energy injuries (type II and III open fractures) may require temporary coverage between serial debridements or until flap coverage. In a prospective, randomized trial, Stannard et al[72] showed that the use of negative-pressure wound therapy (NPWT) between surgical debridements prior to wound closure resulted in a five-fold decrease in infection rate compared with standard gauze dressing. In contrast, Bhattacharyya et al[73] retrospectively reviewed 38 patients with type IIIB open tibial fractures and found that NWPT did not allow coverage delay because there was a significant increase in the infection rates when coverage was delayed beyond a mean of 4.8 days.

Conclusion

The acute management of open fractures remains a challenge to orthopedic surgeons. There is strong evidence that prophylactic antibiotics (eg, a first-generation cephalosporin) should be administered as soon as possible to reduce the risk of deep infection. Urgent operative irrigation and debridement is the standard of care, usually performed during daytime hours by an experienced team. The goals of surgery are to achieve thorough debridement, bone stabilization, and restoration of the soft tissue envelope. Questions persist regarding the optimal irrigation solution and delivery pressure, the timing of wound closure, and the value of post-debridement wound cultures. Multiple fixation techniques are available, each with its advantages and disadvantages. The role of adjunctive therapies, such as antibiotic-impregnated devices, rhBMP-2, and NPWT between serial debridements, is emerging.

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