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Current Concepts Review

Trends in the Management of Open Fractures

A Critical Analysis

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- Antibiotics should be administered to a patient with an open fracture as soon as possible to reduce the risk of infection.
- A patient with an open fracture should be taken to the operating room on an urgent basis, with the stability of the patient, the preparation of the operating room, and the availability of appropriate assistance taken into account.
- Questions remain regarding the optimal solution and method of delivery for irrigation of open fracture wounds.
- Early closure of adequately débrided wounds is safe and can improve outcomes.
- Adjunctive therapies, such as the early application of bone grafts and rhBMP-2, may improve healing of open fractures.

One hundred and fifty years ago, mortality was common following open fracture[1,2]. With the advent of modern therapy, however, the expected outcome has improved dramatically. In the treatment of open fractures, the surgeon's objectives are to prevent infection, promote fracture-healing, and restore function. All patients presenting with an open fracture require initial stabilization, tetanus prophylaxis, systemic antibiotic therapy, prompt surgical débridement and copious irrigation, fracture stabilization, timely wound closure, thorough rehabilitation, and adequate follow-up. In addition, certain patients may benefit from local antibiotic therapy, open wound management (possibly including vacuum-assisted closure), flap closure, bone-grafting, or other adjunctive therapies.

In this review, we analyze the evidence concerning a number of important issues in the management of open fractures, including classification, use of antibiotics, timing of operative intervention, irrigation, fixation, soft-tissue coverage, and adjunctive therapies.

Classification of Open Fractures

A fracture is considered to be open when disruption of the skin and underlying soft tissues results in a communication between the fracture and the outside environment. Open fractures are most commonly classified according to the system developed by Gustilo and Anderson[3] and subsequently modified by Gustilo et al.[4]. According to this system (Table I), type-I open fractures are characterized by a wound of <1 cm with minimal contamination, comminution, and soft-tissue damage. Type II features lacerations of >1 cm and moderate soft-tissue injury, but wound coverage is adequate and periosteal stripping is not extensive. Type-III open fractures are divided into three subtypes. Type IIIA is characterized by high-energy trauma, extensive soft-tissue damage, and substantial contamination, but wound coverage remains adequate after débridement has been completed. Type IIIB is similar to IIIA, except that wound coverage is not adequate and coverage procedures are required. Type IIIC is an open fracture associated with an arterial injury requiring repair. Given the prognostic relevance of soft-tissue and bone injury in the depths of the wound, it is important that open fractures be classified not in the emergency room but in the operating room, after surgical exploration and débridement have been completed.

Recently, the authors of two studies found the Gustilo and Anderson classification system to be associated with low interobserver agreement[5,6]. Brumback and Jones presented 245 orthopaedic surgeons with twelve videotaped case presentations that included patient demographic data, the history of the injury, the results of physical examination, the appearance

TABLE I Classification System of Gustilo et al.[3,4]: Definitions and Associated Infection Rates

Fracture Type	Definition	Historical Infection Rates[3,4,7,8] *(%)*
I	Wound <1 cm; minimal contamination, comminution, and soft-tissue damage	0-2
II	Wound >1 cm; moderate soft-tissue damage, minimal periosteal stripping	2-5
IIIA	Severe soft-tissue damage and substantial contamination; coverage adequate	5-10
IIIB	Severe soft-tissue damage and substantial contamination; coverage inadequate	10-50
IIIC	Arterial injury requiring repair	25-50

of the wound before the operation, preoperative radiographs, and narrated portions of the operative débridement and then asked them to classify the open fractures with use of the Gustilo and Anderson system. The level of agreement (defined as the largest percentage of observers choosing a single classification) averaged just 60%, which the authors characterized as "moderate to poor."[5] However, it is unclear whether these low levels of agreement were due, at least in part, to the fact that the classifications were performed on the basis of videotaped presentations.

In spite of these limitations, the Gustilo and Anderson classification remains the preferred system for categorizing open fractures since the fracture type correlates well with the risk of infection and other complications. For example, rates of infection have been reported to be 0% to 2% for type I, 2% to 5% for type II, 5% to 10% for type IIIA, 10% to 50% for type IIIB, and 25% to 50% for type IIIC[3,4,7,8] (Table I). The number of patients studied in these reports ranged from eighty-seven[4] to 1104[7].

Recently, Bowen and Widmaier[9] studied 174 patients with open fractures of the long bones and found not only the Gustilo and Anderson classification but also the number of compromising comorbidities to be significant predictors of infection in the multivariate analysis. The patients were divided into three classes on the basis of the presence or absence of fourteen medical and immunocompromising factors, including an age of eighty years or more, current nicotine use, diabetes, malignant disease, pulmonary insufficiency, and systemic immunodeficiency. Infection rates were found to be 4% (two of fifty-seven) for patients in Class A (no compromising factors), 15% (thirteen of eighty-nine) for patients in Class B (one or two compromising factors), and 31% (five of sixteen) for patients in Class C (three or more compromising factors) ($p = 0.007$).

Use of Antibiotics

Antibiotic use has been considered the standard of care since 1974, when Patzakis et al. reported their seminal randomized, controlled trial of cephalothin, a first-generation cephalosporin, for the management of open fractures[10]. The benefit of antibiotics was confirmed by a recent Cochrane systematic review[11], which showed that the administration of antibiotics after an open fracture reduces the risk of infection by 59% (relative risk, 0.41; 95% confidence interval, 0.27 to 0.63) (Table II).

Although, in the past, cultures were routinely done before and after débridement of open fractures, authors of recent studies have questioned their utility[12,13]. Lee studied pre-débridement cultures and found that only 8% (eighteen) of 226 organisms grown on culture eventually caused infection and 7% (seven) of 106 patients with negative cultures eventually became infected[12]. Post-débridement cultures were not much better, as only 25% (eight) of thirty-two organisms grown on culture eventually caused infection, and 12% (ten) of eighty-six patients with negative cultures eventually became infected[12]. Currently, we do not recommend the routine use of cultures either before or after débridement (Table II).

As suggested by the above study[12], the organisms that are found to be contaminating an open fracture on presentation do not represent the microbes that will eventually cause infection. In fact, there is evidence that most infections at the sites of open fractures are caused by nosocomial bacteria. In a study carried out by Carsenti-Etesse et al., 92% (thirty-five) of thirty-eight open-fracture infections were caused by bacteria acquired while the patient was in the hospital[14]. Currently, most open-fracture infections are caused by gram-negative rods and gram-positive staphylococci[3,4,12,14]. However, methicillin-resistant *Staphylococcus aureus* has recently emerged as a potential cause of infection of open fractures. During an epidemic at a hospital in Texas during the 1980s, methicillin-resistant *Staphylococcus aureus* developed at the site of an open fracture in twenty-three patients, most of whom had a less than satisfactory outcome[15]. Methicillin-resistant *Staphylococcus aureus* infections of open fractures were also documented in the study by Carsenti-Etesse et al. These developments underscore the importance of early wound coverage.

While there is ample data supporting the administration of antibiotics after open fracture, evidence indicating an optimal regimen is lacking. In the randomized, controlled trial by Patzakis et al.[10], patients receiving the first-generation cephalosporin cephalothin were found to have a lower infection rate than those receiving penicillin and streptomycin (2.3% compared with 9.7%). In a later study by the same group of researchers, therapy with cefamandole and tobramycin was found to be superior to penicillin and streptomycin (4.5% compared with 10%), but not better than monotherapy with cephalothin (5.6%)[7]. Also of interest is the prospective double-blind study by Benson et al., who found clindamycin to be as effective as cefazolin for preventing infection after open fracture[16].

Ciprofloxacin has also been considered for the management of open fractures, given its activity against both gram-

positive and gram-negative organisms. Patzakis et al. conducted a prospective, double-blind, randomized, controlled trial comparing monotherapy with ciprofloxacin to combination therapy with cefamandole and gentamicin and found the two types of therapy to be associated with similar infection rates in patients with a type-I or II fracture but the use of ciprofloxacin to be associated with a higher rate of infection in those with a type-III fracture (31% [eight of twenty-six] compared with 7.7% [two of twenty-six]; $p = 0.08$)[17]. While a number of recent animal and in vitro studies have suggested that ciprofloxacin and other fluoroquinolones may act to inhibit osteoblast activity and fracture-healing[18,19], further investigation—especially in the clinical setting—is required before the use of these antibiotics is discouraged for the management of open fractures.

There is currently controversy with regard to the specific antibiotic agent(s) to be given after open fracture. While some have recommended treating all open fractures with a combination of a first-generation cephalosporin and an aminoglycoside[20], others have advocated monotherapy with a first-generation cephalosporin for type-I and II fractures with the addition of an aminoglycoside (usually gentamicin) for type-III fractures[21]. Most agree that penicillin or ampicillin should be added when there is a high risk of anaerobic infection (in association with farm injuries, for example).

TABLE II Recommendations for the Management of Open Fractures

Recommendation	Grade of Recommendation*
Antibiotics	
Systemic therapy	A
Local therapy	B
Timing of operative débridement	
Urgent	B
Within 6 hr	C
Irrigation	
High-pressure pulsatile lavage	I
Additives†	I
Fixation	
Femur (intramedullary nailing)	B
Tibia	
External fixation	B
Intramedullary nailing	B
Reaming	I
Coverage and closure	
Primary closure	B
Vacuum-assisted closure	I
Adjunctive therapies	
Early prophylactic bone-grafting	C
Local rhBMP-2	B
Modalities not recommended	
Wound culture	B

*A = Good evidence (Level-I studies with consistent findings) for or against recommending intervention, B = fair evidence (Level-II or III studies with consistent findings) for or against recommending intervention, C = poor-quality evidence (Level-IV or V studies with consistent findings) for or against recommending intervention, and I = there is insufficient or conflicting evidence not allowing a recommendation for or against intervention. †Antibiotic, antiseptic, or soap additives.

The available evidence suggests that antibiotic treatment should be initiated as soon as possible following injury. In a study of 1104 open fractures, Patzakis and Wilkins reported an infection rate of 4.7% (seventeen of 364) when antibiotics were given within three hours after the injury compared with a rate of 7.4% (forty-nine of 661) when therapy was begun more than three hours after the injury (seventy-nine patients did not receive antibiotics)[7]. The optimal duration of antibiotic therapy is less clear. Many authors have recommended an initial three-day course supplemented by additional three-day courses at the time of any subsequent procedures[20], although clinical evidence to support this approach is lacking. Dellinger et al. advocated a one-day course of antibiotics on the basis of a prospective, double-blind, randomized, controlled trial that showed a single day of antibiotics to be as effective as a five-day regimen for preventing infection[22].

At our institution, we recommend the administration of cefazolin (1 g intravenously) every eight hours until twenty-four hours after the wound is closed. Intravenous gentamicin (with weight-adjusted dosing) or levofloxacin (500 mg every twenty-four hours) are added for type-III fractures.

Over the past decade, interest has grown in the use of local antibiotic therapy to prevent infection after open fracture. Local therapy has been shown to generate high antibiotic concentrations within the wound while maintaining low systemic concentrations[23], which reduces the risk of systemic side effects. Antibiotic agents that are heat-stable, available in powder form, and active against suspected pathogens are appropriate choices for local therapy. While aminoglycosides and vancomycin both meet those criteria, the former is preferred because of concerns about encouraging resistance to vancomycin.

While very high concentrations of aminoglycosides can certainly impair osteoblast function, early in vitro studies have suggested that this toxicity threshold was on the order of several hundred micrograms per milliliter, well above the concentrations of 10 to 20 μg/mL typically seen in the wound[24]. However, a recent study by Ince et al.[25] suggested that the toxicity threshold may actually be much lower, on the order of 12.5 μg/mL. This finding should be further investigated in future studies.

Use of aminoglycoside-eluting polymethylmethacrylate beads has been studied by several investigators. Ostermann et al. conducted a retrospective analysis of 1085 open fractures and found that patients treated with tobramycin-eluting beads had a significantly lower rate of infection (3.7% [thirty-one of 845]) than did those not treated with the beads (12.1% [twenty-nine of 240]; $p < 0.001$)[26]. However, wounds treated with local antibi-

otic therapy were also more likely to be closed earlier in the study, which introduces the possibility of bias. Keating et al. conducted a retrospective analysis of eighty-one open tibial fractures and found tobramycin-eluting beads to be associated with a lower risk of infection (4% [two of fifty] compared with 16% [four of twenty-five]), although the result was not significant, at least partly as a result of a small sample size[27]. Recently, some authors have investigated the use of local antibiotic therapy alone. Moehring et al. conducted a prospective, randomized, controlled trial comparing local and systemic antibiotic therapy in the management of type-II, IIIA, and IIIB open fractures[28]. After receiving standard treatment in the emergency room and operating room (including an initial dose of systemic antibiotics), patients were randomized to receive either local therapy with tobramycin-eluting beads or systemic therapy with a first-generation cephalosporin. Similar rates of infection were reported in the two groups (8% [two of twenty-four] compared with 5% [two of thirty-eight], respectively). However, the study was not adequately powered (it had a small sample size), and a substantial proportion of the study population (15%) was inadvertently treated with both interventions.

We consider local antibiotic therapy to be a useful adjunct to systemic antibiotics in the management of open fractures (Table II). While gentamicin-impregnated beads are commercially available in Europe, antibiotic-eluting polymethylmethacrylate cement is not yet available in bead form in the United States. Instead, antibiotic beads can be made by mixing polymethylmethacrylate cement with tobramycin powder at a dose of 3.6 g per 40 g of cement[29].

Recently, a number of animal studies have suggested the potential utility of other forms of local antibiotic therapy, including the use of antibiotic-impregnated bone graft[30], antibiotic-impregnated bone-graft substitute[31-33], and antibiotic-coated intramedullary nails[34]. However, these innovations have yet to be studied in a clinical setting, to our knowledge.

Timing of Operative Treatment

Emergency operative treatment has long been the standard of care for open fractures. The origin of the so-called "six-hour rule" is unclear, however. While some believe that it stems from an 1898 experiment by Friedrich, in which guinea pigs with contaminated soft-tissue wounds had lower rates of infection when débridement was performed within six hours[35], others point to a 1973 study by Robson et al., who reported that 10^5 organisms per gram of tissue was the open-fracture infection threshold, which was reached in an average of 5.17 hours[36].

To date, two studies have shown a decreased rate of infection when débridement is performed within six hours. In a study of forty-seven open tibial fractures, Kindsfater and Jonassen found that operative treatment within five hours was associated with a lower risk of infection (7% [one of fifteen]) compared with 38% [twelve of thirty-two]; $p < 0.03$)[37]. However, severe fractures were more likely to be treated later in this study: type-III fractures accounted for 33% (five) of the fifteen fractures treated within five hours but 53% (seventeen) of the thirty-two treated after a delay of five hours or more. Kreder and Armstrong found that, of fifty-six open tibial fractures in children, the forty-two that had been treated within six hours had a lower rate of infection (12% [five infections]) than the eight that had been treated after a delay of more than six hours (25% [two infections])[38]. However, the study was limited by its small sample size (just one fewer infection in the delayed-treatment group would have resulted in identical rates of infection).

A number of studies have called the "six-hour rule" into question[7,39-46]. Bednar and Parikh reviewed the results associated with eighty-two open tibial and femoral fractures and found no significant differences between those débrided within six hours and those débrided at seven hours or later (9% compared with 3.4%; $p > 0.05$)[40]. Ashford et al. reported on open tibial fractures among patients from the Australian outback, many of whom were unable to reach medical care within six to eight hours after the injury because of issues related to distance[39]. The authors found no difference in infection rates between those treated within six hours and those treated after six hours (17% [two of twelve] compared with 11% [four of thirty-six]; $p > 0.05$). Spencer et al., who prospectively studied 142 open long-bone fractures in the United Kingdom, also reported no significant difference in infection rates between those treated within six hours and those treated after six hours (10.1% [seven of sixty-nine] compared with 10.9% [five of forty-six]; $p > 0.05$)[45]. Additionally, Pollack and the LEAP investigators studied 315 open fractures of the lower extremity and found that the time from the injury to the first débridement did not correlate with the likelihood of infection[46]. It is interesting to note, however, that patients who had been admitted to a hospital within six hours after the injury had a lower prevalence of infection than those who had been admitted after six hours (22% compared with 39%; $p < 0.01$).

One must use caution, however, when drawing conclusions from these reports. Since the studies were not randomized, there is the potential for bias; the fact that severe fractures were more likely to be treated urgently could, for example, artificially raise the infection rates in the groups treated within six hours while artificially decreasing the rates in the groups treated after six hours. Additionally, many of the studies were not adequately powered, with sample sizes too small to enable detection of a clinically meaningful difference in infection rates.

A few authors have gone so far as to suggest that operative débridement might not be necessary for low-grade open fractures[47,48]. Orcutt et al. conducted a retrospective study comparing ninety-nine low-grade (type-I and II) open fractures managed with local wound care and intravenous antibiotics (but no operative débridement) with fifty similar fractures managed with formal operative débridement as well as intravenous antibiotics[47]. They found lower rates of infection (3% compared with 6%) and delayed union (10% compared with 16%) in the nonoperative group, but these differences were not significant ($p > 0.05$). More recently, Yang and Eisler reported favorable outcomes, including an infection rate of 0%, in a retrospective study of ninety-one type-I open fractures managed

without formal operative débridement[48]. However, the authors acknowledged the difficulty of correctly predicting fracture severity on the basis of superficial characteristics alone and noted that many fractures that had been initially labeled type I at their institution were subsequently reclassified at the time of operative débridement.

In our opinion, thorough operative débridement should be considered the standard of care for all open fractures. Even if the benefits of formal débridement were found to be insignificant for low-grade open fractures, operative débridement would still be required for proper classification of the wound. As noted above, open fractures graded on the basis of superficial characteristics alone are often misclassified. Thus, failure to adequately explore and débride an open fracture in the operating room is associated with substantial risk.

In contrast, it is not possible at this point in time to argue for or against a firm "six-hour rule" in the management of open fractures. In the prevention of infection after open fracture, the time from injury to débridement is probably less important than other factors, such as the adequacy of débridement and the timeliness of soft-tissue coverage. Patients with an open fracture should be taken to the operating room on an urgent basis, with the stability of the patient, the preparation of the operating room, and the availability of appropriate assistance (including orthopaedic-trained scrub personnel, assistant surgeons, radiography technicians, and other operating-room personnel) taken into account (Table II).

Wound Irrigation

Irrigation is a key component of the effort to prevent infection after open fracture, as it serves to decrease bacterial load and remove foreign bodies. Although many guidelines call for so-called "copious" amounts of irrigation, there are little data on exactly how much volume should be used in the lavage of open fracture wounds. As irrigation bags typically contain 3 L of fluid, some have recommended 1 bag (3 L) for type-I open fractures, two bags (6 L) for type-II, and three bags (9 L) for type-III[49].

With regard to the delivery of irrigation, high-pressure pulsatile lavage appears to be most effective for the removal of bacteria and other contaminants. With a standard battery-operated pulsatile irrigation system (e.g., Surgilav Plus Debridement System, Stryker Instruments, Kalamazoo, Michigan), high-pressure pulsatile lavage corresponds to a pressure of 70 lb psi with 1050 pulsations per minute (as opposed to 14 lb psi and 550 pulsations per minute for low-pressure pulsatile lavage). Anglen et al.[50] found that high-pressure pulsatile lavage increased the removal of slime-producing bacteria from stainless-steel screws by a factor of 100. In a study of an in vitro tibial model, Bhandari et al.[51] found that, although high and low-pressure pulsatile lavage were equally successful in removing bacteria after a delay of three hours, only high-pressure lavage was successful after a delay of six hours.

There is increasing evidence from animal and in vitro studies that high-pressure pulsatile lavage may have deleterious side effects[51-55]. In the in vitro study by Bhandari et al., for example, high-pressure pulsatile lavage caused significantly more macroscopic bone damage than low-pressure pulsatile lavage ($p < 0.001$)[51]. In addition, histologic analysis showed high-pressure pulsatile lavage to be associated with cortical bone defects that were significantly larger and more numerous than those resulting from low-pressure pulsatile lavage ($p < 0.001$). In a study of rats, Adili et al. found high-pressure pulsatile lavage of open noncontaminated femoral diaphyseal fractures to be associated with reduced mechanical strength at three weeks (but not at six weeks)[52]. In addition, Hassinger et al. found high-pressure lavage to be associated with increased depths of bacterial penetration in sheep muscle[55]. To our knowledge, however, there have been no clinical studies of high or low-pressure pulsatile lavage for the irrigation of open fracture wounds. Thus, there is insufficient evidence to make a recommendation with regard to the delivery of irrigation (Table II).

Sterile saline solution, either alone or with an additive, is commonly used for the irrigation. The available additives can be divided into three general categories: antiseptics, such as povidone-iodine (Betadine), chlorhexidine gluconate (Hibitane), and hexachlorophene (pHisoHex); antibiotics, such as bacitracin; and soaps, which function by removing microbes (instead of killing them). These solutions have been compared in a number of animal and in vitro studies[50,56,57]. In the study by Anglen et al., soap solutions were found to be most effective in removing slime-producing bacteria from stainless-steel screws, whereas antibiotic solutions were not significantly different from normal saline solution ($p > 0.05$)[50]. Bhandari et al. compared various irrigation solutions in an in vitro model and found that, while povidone-iodine, chlorhexidine gluconate, and liquid soap were most effective in removing bacteria from bone, soap had the least injurious effect on osteoblast and osteoclast function[56].

Recently, Anglen reported the results of a prospective, randomized, controlled trial comparing nonsterile castile soap with bacitracin solution for the irrigation of 398 lower-extremity open fractures[58]. The two solutions contained 80 mL of liquid castile soap (Triad Medical, Franklin, Wisconsin) or 100,000 units of bacitracin (Baciim; Pharma-Tek, Huntington, New York) in a 3-L bag of saline solution. The irrigation volume varied by fracture grade (3 L for type I, 6 L for type II, and 9 L for type III) and was delivered by a power irrigator system (Pulsavac; Zimmer, Dover, Ohio). No significant differences with respect to infection and bone-healing were found, but wound-healing problems were more common in the bacitracin group (9.5% [nineteen of 199] compared with 4% [eight of 199]; $p = 0.03$). Since the study was adequately powered, the failure to detect a significant difference in the rates of infection was probably not related to issues of small sample size. Therefore, given the available evidence, it is not possible to recommend any particular additive for the irrigation of open fracture wounds (Table II).

Role of Fixation

Fixation of open fractures has a number of beneficial effects, including protection of soft tissues from additional injury by

fracture fragments, improvement of wound care and tissue-healing, promotion of mobilization and rehabilitation, and possibly even reduction of the risk of infection[59]. In the multiply-injured patient, fracture fixation also reduces the risk of acute respiratory distress syndrome and multiple organ failure, probably by calming the systemic inflammatory response[60]. A number of methods are available for stabilization of open fractures, including splinting, cast immobilization, or traction; external fixation; plates and screws; and intramedullary nailing (with or without reaming). Intramedullary nails may be solid, hollow slotted, or cannulated, with the solid nails demonstrating a greater resistance to infection in animal studies[61,62].

In any given situation, the best option for fixation depends on a number of factors, including the bone involved, the fracture site, the wound location, and the condition of the patient.

Femur

At this point in time, there is consensus regarding the stabilization of open fractures of the femoral diaphysis. Most surgeons advocate early intramedullary nailing with reaming, and there is sufficient evidence to support this approach (Table II). In 1989, Brumback et al. conducted a study of eighty-nine open femoral fractures treated with reamed intramedullary nailing and documented no infections in association with sixty-two type-I, II, and IIIA fractures and only three infections (11%) in association with twenty-seven type-IIIB fractures[63]. Moreover, the rates of infection did not differ between the patients treated within twenty-four hours after injury (early) and those treated after forty-eight hours (late). That same year, Bone et al. reported on a prospective, randomized, controlled trial comparing early stabilization (within twenty-four hours) and late stabilization (after forty-eight hours) of 178 open and closed femoral fractures[64]. While no differences were observed among patients with an isolated femoral fracture, multiply-injured patients were found to have a decreased rate of pulmonary complications (acute respiratory distress syndrome, fat embolism, and pneumonia), a shorter hospital stay, and less time in the intensive-care unit when stabilization had been performed within twenty-four hours. Since that time, a number of other studies have confirmed the favorable outcomes associated with early intramedullary nailing of open femoral shaft fractures[65-67]. In a small study of fifteen patients treated with external fixation with secondary intramedullary nailing of an open femoral shaft fracture, Wu and Shih reported that infection developed in two patients and union occurred in fourteen[68].

Tibia

The optimal treatment of open fractures of the tibial shaft is less clear. During the late 1980s, a number of studies demonstrated favorable outcomes with external fixation. Bach and Hansen conducted a prospective, randomized, controlled trial comparing external fixation with internal fixation with plates and found that, although both methods yielded favorable outcomes, external fixation was associated with fewer complications[69]. At approximately the same time, Edwards et al. reported the results of a prospective study of 202 type-III open tibial fractures treated with external fixation and concluded that that method was successful for the treatment of severe open tibial fractures[70].

During the 1990s, a number of studies showed intramedullary nailing to be preferable to external fixation. Henley et al. prospectively studied 174 open tibial fractures (types II, IIIA, and IIIB) and found unreamed intramedullary nailing to be associated with a lower prevalence of malalignment (8% [eight of 104] compared with 31% [twenty-two of seventy] following external fixation; $p < 0.001$), fewer subsequent procedures (mean, 1.7 compared with 2.7; $p = 0.001$), and a lower rate of infection (13% [thirteen of 104] compared with 21% [fifteen of seventy]; not significant at $p = 0.73$)[71]. Schandelmaier et al. retrospectively reviewed the results of treatment of 114 tibial shaft fractures with severe soft-tissue injury and found unreamed nailing to be associated with fewer subsequent procedures than were seen after external fixation (mean, 0.81 compared with 1.84; $p < 0.001$) and a better functional outcome (mean Karlstrom outcome score, 31.4 compared with 29.6; $p < 0.02$)[72]. Finally, Tornetta et al. conducted a prospective, randomized, controlled trial comparing unreamed intramedullary nailing with external fixation of type-IIIB open fractures of the tibial shaft[73]. Although a small sample size (twenty-nine fractures) prevented the detection of any significant differences, the authors concluded that nailing was preferable because of a perception of easier management and increased patient satisfaction.

In recent years, the debate has centered on whether intramedullary nailing should be performed with or without reaming. While reaming is known to have distinct advantages in the treatment of closed tibial fractures—including a shorter time to fracture-healing, a lower prevalence of nonunion, and less screw breakage[74,75]—studies of animals have shown it to be associated with greater reductions in cortical bone blood flow[76]. This is of particular concern in open tibial fractures, where soft-tissue disruption has already compromised blood supply, which is crucial for wound-healing and the prevention of infection.

Studies comparing reamed and unreamed nailing in patients with an open tibial fracture have proved inconclusive. Keating et al. conducted a prospective, randomized, controlled trial of eighty-eight open tibial fractures treated with either reamed or unreamed intramedullary nailing and found no significant differences with regard to rates of infection or nonunion or functional outcome, although screw breakage was significantly less common in the group treated with reaming ($p = 0.014$)[77]. Finkemeier et al. found no significant differences between reamed and unreamed nailing with regard to union, number of additional procedures, or infection in a prospective, randomized, controlled trial of forty-five open tibial fractures ($p > 0.05$)[78]. Ziran et al. retrospectively reviewed the results in fifty-one patients with an open tibial fracture and found similar rates of nonunion and infection in the two treat-

ment groups but a decreased rate of secondary procedures in the group treated with reaming (41% [nine of twenty-two] compared with 69% [twenty of twenty-nine]; $p < 0.05$)[79]. Given that this failure to detect significant differences between the results of reamed and unreamed intramedullary nailing could be due to small study size (inadequate power), it is worthwhile noting that a recent meta-analysis conducted by Bhandari et al. also failed to demonstrate any significant differences with regard to infection, nonunion, or reoperations[80]. A definitive study comparing reamed and unreamed nailing is currently under way, but the results have not yet become available. At the current time, it is not possible to make a recommendation for or against reaming in the fixation of open tibial fractures (Table II).

Wound Coverage and Closure

Historically, the closure of open fracture wounds has been delayed to prevent infection with Clostridium and other contaminating organisms. While this strategy remains the generally accepted approach in settings characterized by substantial contamination (such as the barnyard and the battlefield), many orthopaedic surgeons practicing in the developed world have begun to consider earlier closure of open fracture wounds that have been adequately débrided. In this setting, where nosocomial organisms have emerged as the main source of open-fracture infections[14], several studies have documented significantly better outcomes with early closure (within seven days) than with late closure ($p < 0.05$)[81-84]. Also, a number of studies have demonstrated excellent outcomes with closure performed within three days after injury[85,86].

Recently, a number of authors have investigated the feasibility of immediate closure (within twenty-four hours after injury). In a study of 119 open fractures, DeLong et al. did not find immediate closure (within twenty-four hours) to be associated with a higher rate of infection or nonunion when compared with delayed closure (at more than twenty-four hours)[87]. Gopal et al. retrospectively reviewed the results associated with eighty-four type-IIIB and IIIC open tibial fractures treated with immediate internal fixation and flap closure and reported lower rates of infection and amputation as well as a shorter time to union when compared with the outcomes of early closure (at twenty-four to seventy-two hours) and late closure (at more than seventy-two hours), although significance was not assessed[88]. Finally, Hertel et al. performed a retrospective study of twenty-nine type-IIIA and IIIB open tibial fractures and found that immediate coverage was associated with a lower rate of infection (0% [zero of fourteen] compared with 27% [four of fifteen] after later coverage; $p = 0.04$), a reduced number of reoperations (mean, 1.6 compared with 3.9; $p = 0.0001$), and a decreased time to definitive union (mean, 5.6 months compared with 11.6 months; $p = 0.005$)[89]. In our opinion, early closure of thoroughly débrided wounds is safe and can improve outcomes (Table II).

Of note, the trend toward early closure of open fractures conflicts with recommendations for routine débridement of open fractures[21]. While the goal is thorough débridement at the time of the initial presentation, it is possible that polytrauma or other concerns may cause the surgeon to doubt the adequacy of the initial débridement. In addition, it may be difficult to evaluate muscle viability in the acute setting. In these instances, repeat débridement is certainly appropriate.

There are a number of methods for achieving closure, including direct suturing, split-thickness skin-grafting, and use of free or local muscle flaps. The optimal method depends on a number of factors, including the location of the defect, its size, associated injuries, and patient characteristics such as the amount of function retained and the desired level of function.

Recently, vacuum-assisted closure (V.A.C.; KCI, San Antonio, Texas) has emerged as a useful method of accelerating wound-healing by reducing chronic edema, increasing local blood flow, and enhancing granulation tissue formation[90,91]. A small number of reports have documented the use of vacuum-assisted closure in the management of orthopaedic wounds, with generally favorable results[92-95]. For example, DeFranzo et al. reported on the use of vacuum-assisted closure in the treatment of seventy-five lower-extremity wounds with exposed bone and found it to be successful in reducing tissue edema, shrinking wound size, and stimulating granulation tissue formation[92]. In a retrospective review, Labler et al. compared vacuum-assisted closure with use of the synthetic membrane Epigard (Biovision, Ilmenau, Germany) in the management of type-IIIA and IIIB open fractures of the lower extremity[94]. Vacuum-assisted closure was associated with favorable outcomes, and it resulted in a lower rate of infection when compared with the Epigard (two of thirteen compared with six of eleven). The vacuum-assisted-closure device is typically applied at the end of each irrigation and débridement until the wound is considered clean. After that point, sponges can be changed at the bedside every two to three days. Vacuum-assisted closure was used for an average of ten to twenty days in the studies described above. While vacuum-assisted closure appears to be a promising modality in the management of musculoskeletal wounds, additional studies are required before a definitive recommendation can be made (Table II).

Adjunctive Therapies

There is evidence that certain adjunctive therapies may be useful in the management of open fractures. Early prophylactic bone-grafting, which is typically performed within twelve weeks after injury (but not before two weeks after wound closure), has been shown to be useful in a small number of studies. Blick et al. conducted a retrospective review of fifty-three high-energy tibial fractures (mostly type III) that had been treated prophylactically with posterolateral bone-grafting within ten weeks after the injury (eight weeks after soft-tissue coverage)[96]. Patients treated with early prophylactic bone-grafting had a shorter time to bone union compared with historical controls (mean, 45.7 weeks compared with 57.4 weeks; $p = 0.03$). Similarly, Trabulsy et al., in a prospective study of forty-five type-IIIB open tibial fractures, found that patients who had been treated with bone-grafting within eight to twelve weeks after injury had a shorter time to osseous union

(mean, forty-one weeks compared with fifty-two weeks; p value not reported)[97]. However, given that external fixation was the primary means of fracture stabilization in these studies, one must use caution when generalizing the results to open tibial fractures treated with intramedullary nailing. Additional studies are required before a definitive recommendation can be made regarding the use of early prophylactic bone-grafting in the management of open fractures (Table II).

Recently, evidence has emerged regarding the use of recombinant human bone morphogenetic protein-2 (rhBMP-2). In a multicenter, prospective, randomized, controlled trial of 450 open tibial fractures, the use of local rhBMP-2 implants was found to significantly reduce the risk of secondary invasive interventions (26% compared with 46%; risk ratio = 0.56; 95% confidence interval = 0.40 to 0.78; p = 0.0005). Patients treated with rhBMP-2 also had a lower rate of hardware failure (11% compared with 22%; p = 0.0476), faster fracture-healing (median healing time, twenty compared with fifty-two weeks), and faster wound-healing (83% compared with 65% healed at six weeks; p = 0.001)[98]. Treatment of type-IIIA and IIIB open fractures with rhBMP-2 was associated with a significantly lower risk of infection (21% compared with 40%; p = 0.0234) as well as secondary procedures (9% compared with 28%; p = 0.0065) and bone-grafting (2% compared with 20%; p = 0.0005)[99]. Among patients who were treated with reamed intramedullary nailing (all fracture types included), use of rhBMP-2 was associated with a trend toward lower rates of invasive secondary procedures (8% [five of sixty-five] compared with 15% [seven of forty-eight]) and bone-grafting (2% [one of sixty-five] compared with 6% [three of forty-eight]), but the results were not significant (p = 0.35 and 0.31, respectively). Given that these subgroup analyses were not adequately powered and were performed post hoc, however, one must use caution when drawing conclusions. While additional studies are certainly required, there does appear to be fair evidence in support of the use of rhBMP-2 in the management of open fractures, especially those of severe grade (Table II).

Overview

Open fractures represent a challenge to even the most experienced orthopaedic surgeons. Antibiotics should be administered as soon as possible. Early operative débridement remains essential, although there is limited evidence in support of a firm "six-hour rule." Copious irrigation is crucial, but questions remain regarding the optimal solution and method of delivery. Early internal fixation is safe and has a number of benefits, with the optimal method of stabilization depending on the bone involved and other factors. The available evidence supports the current trend toward earlier coverage and closure of open fracture wounds. Vacuum-assisted closure appears to decrease wound size and improve healing, but additional studies are required in the field of orthopaedics. Adjunctive therapies, such as the use of early prophylactic bone-grafting and recombinant human bone morphogenetic protein-2 (rhBMP-2), may improve bone-healing and other outcome measures (Table II).

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