

The Management of Complications Associated With Tibial Fractures

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Abstract

Tibial fractures are common and frequently require surgical stabilization. These two factors mean that complications when treating this difficult injury are to be expected. The objectives in the treatment of open tibial shaft fractures are to prevent sepsis, achieve union, and restore function of the limb. However, these goals are often compromised by infection, compartment syndromes, and bone loss associated with many tibial shaft fractures.

Recent studies provide a better understanding of the factors involved in the initial care of patients with open tibial fractures and have challenged prior dogmas and practices. An example is studies that define the relationship between the time to débridement of open fractures and subsequent infection. The diagnosis of compartment syndromes continues to be challenging. Careful review of clinical criteria will assist physicians in the early recognition and the management of compartment syndromes. Despite uncomplicated initial care, infections will occur. However, improved knowledge in the basic science of infections, specifically infections about orthopaedic implants, has led to the development of protocols for treatment and obtaining union.

Bone loss, a result of either infection or trauma, is one of the most difficult complications to manage. Research regarding bone morphogenesis and the synthesis of multiple compounds has created new options for treating tibial fractures with bone loss.

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Gustilo's "imperatives" for the treatment of open tibial fractures included (1) no primary closure of type III open fractures; (2) the use of antibiotics; and (3) consideration of open

fractures as emergencies. This historical dogma recently has been challenged, particularly the timing of débridement. The Lower Extremity Assessment Project (LEAP)

study¹ documented an overall infection rate of 27%, and analysis revealed that there was no difference in the rates of infection when the time to the initial irrigation and débridement and the time to definitive wound coverage were compared. In wounds closed less than 6 hours after injury, the infection rate was 22.2%; in wounds closed later than 6 hours, the infection rate was 38.9%. These values were not statistically different. A recent study by Skaggs and associates² evaluated 536 consecutive patients treated at six pediatric trauma referral centers (Table 1). There was no difference in the rates of infection for open fractures that received an initial irrigation and débridement in less than 6 hours compared with fractures in which the initial irrigation and débridement was done after 6 hours. This study is similar to other published studies analyzing rates of infection in the treatment of open fractures based on early or delayed closure^{3,4} (Table 2). Although all of these studies apparently show no difference in the rates of early and late wound closure, a power analysis

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Table 1
The Effect of Surgical Delay on Acute Infection Following 554 Open Fractures in Children*

Gustilo Type	< 6 Hours to Irrigation and Débridement	> 6 Hours to Irrigation and Débridement
I	2%	2%
II	3%	0%
III	10%	6%
Total	3%	2%

*Retrospective, multicenter study of open fractures treated at six tertiary pediatric medical centers from 1989 to 2000; 554 open fractures in 536 consecutive patients.

Table 2
Rates of Infection Based on Early or Delayed Closure

Study	Number of Open Fractures	Early Irrigation and Débridement	Late Irrigation and Débridement
Skaggs et al ²	554	3%	2%
Bednar and Parikh ³	82	5%	5%
Patzakis and Wilkins ⁴	1025	4.7%	7.4%

to rule out type II error (beta error) was not conducted.

Recent *in vitro* studies indicate that *Staphylococcus aureus* is rapidly translocated into osteoblasts. This may explain why some of the effects of antibiotics are negated when antibiotics are administered later than 12 hours after infection. Patzakis and Wilkins⁴ and Bosse and associates⁵ consistently state that the most important factor for preventing infection is the early administration of antibiotics providing gram-positive and gram-negative coverage.

Management of the Open Tibial Fracture Wound

The first decision to make when evaluating an open tibial fracture is to determine if the extremity is salvageable. To do this, the vascularity of the limb must be assessed. If the limb is ischemic, the warm ischemia time must be known to determine if the tissues distal to the ischemia are salvageable. In a multiply injured patient, associated injuries may lead

to amputation rather than limb salvage. In a patient who is dying from blood loss, amputation may be a life-saving procedure, allowing control of hemorrhage. The general health of the patient, when it can be assessed, is an important aspect during evaluation of the mangled extremity. The surgeon should consider the magnitude of the reconstructive effort in comparison with a patient's ability to tolerate the reconstruction, along with ultimate functional outcomes. The LEAP study found no difference between amputation and salvage for high-grade, open lower extremity fractures at 2 and 7 years.¹ The investigators did find that reconstruction or limb salvage patients had more surgeries than those who underwent amputation and that lack of plantar sensation on presentation was not predictive of failed reconstruction. Half of the patients who had no plantar sensation recovered it later. Another somewhat surprising finding of the LEAP study was that

through-the-knee amputation had a worse functional outcome than below-knee or above-knee amputations. Once the decision has been made to salvage a limb, wound treatment goals are to remove all foreign materials and devitalized host tissue and reduce the bacterial contamination load, which is done with irrigation and débridement.

Several parameters of irrigation should be considered, including volume, pressure, pulsatile flow, and additives. Increased fluid volume will remove more particulate debris from wounds; however, a plateau often is reached when increased fluid volume will not remove more debris. One empiric protocol for irrigation volume is based on the grade of the wound and suggests that a Gustilo type I wound should be irrigated with 3 L of fluid, a type II wound with 6 L, and a type III wound with 9 L. Increasing pressure of irrigation does remove more debris, but high irrigation pressures can damage bone, drive debris into tissues, and delay healing through damage to soft tissues. Medium or moderate pressures should be used. Pulsatile flow is of no proven value.⁶

A variety of different irrigation solutions have been used, including antiseptics, antibiotics, and detergents. Antiseptics, including povidone-iodine, peroxide, alcohol, chlorhexidine, and hexachlorophene generally are toxic to both bacteria and host cells. In most instances, they are just as toxic to the host's immune cells as they are to bacteria and may actually worsen the situation by damaging host tissues. Irrigation with antiseptics has no proven efficacy in any human fracture study. Antibiotic additives are not proven to reduce infection in any human studies of traumatic wounds or open fractures.⁶ Soaps

have been used to cleanse wounds for hundreds of years, and extensive laboratory data suggest that surfactants (detergents) are effective at reducing recoverable bacteria in contaminated animal models.¹ In clinical practice, 8 mL of liquid castile soap (nonsterile) in a 3-L bag of irrigation saline can be used as a surfactant. A prospective randomized controlled trial suggested that soap solution was equal to antibiotic bacitracin solution at preventing infection and may be less detrimental to soft-tissue wound healing.⁷

Débridement is important in preventing infection. It requires careful judgment and should be done by, or at least under the guidance of, the most experienced member of the surgical team, because initial mistakes are not easily corrected.

Several technical points about débridement can be emphasized. First, a tourniquet should be placed on the limb; however, tourniquet use should be judicious. Ischemia is to be avoided. Bleeding is an important sign of tissue viability and should not be obscured by excessive tourniquet use. Débridement should begin at the most superficial layer and proceed systematically toward the deeper layers. Often, adequate exploration of the wound requires extension of the traumatic lacerations. Extension of the wound should be done before débridement begins. Incisions and wound extensions should be planned to accommodate future surgery or flaps needed for soft-tissue closure. All foreign material must be removed and the wound thoroughly inspected at the initial surgery to make sure that no foreign material is left behind.

Repeat irrigation and débridement procedures at 24- to 48-hour intervals are done until the wound is clean and healthy. During this time, the tissue

should be kept covered, moist, and protected until definitive closure is achieved. Definitive closure or coverage of the wound should occur within 1 week if possible. Primary closure of open fracture wounds is controversial, but many surgeons believe it is acceptable for clean wounds without necrotic tissue, particularly low-grade wounds, or after radical débridement of higher grade injuries.

The methods of interim wound coverage include application of a semipermeable membrane or artificial skin, use of an antibiotic bead pouch, or vacuum-assisted closure (VAC). Use of a wet-to-dry dressing should be avoided whenever possible because desiccation is detrimental to tissues.

The antibiotic bead pouch for open fractures was described by Seligson and associates at the University of Louisville in 1984.⁸⁻¹⁰ This technique allows delivery of a high concentration of antibiotics to local tissues with low systemic levels. It also prevents wound desiccation. The use of the antibiotic bead pouch technique is indicated for highly contaminated fractures, grade III fractures, open wounds with bone defects, and osteomyelitis after débridement.

The technique of antibiotic bead pouch placement involves the use of polymethylmethacrylate (PMMA) bone cement with antibiotics added. The beads can be formed in a mold or can be rolled by hand and placed on a wire or suture. The antibiotics selected must be heat stable, water soluble, wide spectrum, and available in powder form and must have a low incidence of allergic reaction. Choices have included aminoglycosides (gentamicin and tobramycin), cephalosporins, and vancomycin. The antibiotic powder is added to the PMMA powder before mixing.

In one recipe, 2.4 g of tobramycin powder is added to a 40-g pouch of PMMA. Although some authors have used as much as 9.6 g of tobramycin powder per bag of PMMA, an excessive amount of antibiotic will impair cement hardening.¹⁰

After thorough débridement and irrigation, the beads are packed in the wound and in the bone defect, and then covered with a semipermeable membrane (for example, Tegaderm [3M, St. Paul, MN], Opsite [Smith & Nephew, Hull, England] or Epigard [Ormed, Freiburg, Germany]) that allows diffusion of oxygen but not water vapor. Some surgeons use an overflow drainage tube and the antibiotic bead pouch. Suction drains should not be used because removal of the antibiotic-containing fluid would be counterproductive. The beads are kept in place until repeat visits to the operating room are planned.

Outcome studies on the use of an antibiotic bead pouch suggest that open fractures treated with this technique have a lower overall infection rate than historical controls. Prospective, randomized, placebo-controlled studies with adequate numbers have not been done. Animal studies suggest that antibiotic bead pouches are as good as or better than systemic antibiotics in preventing infection.^{11,12} In most human studies, the two techniques have been used simultaneously.

VAC is a widely used technique for the care of open fracture wounds in the tibia.^{13,14} The VAC exposes the wound to subatmospheric pressure, removing fluid from the wound and from the interstitial spaces. It prevents wound desiccation, improves circulation, enhances granulation tissue, and lowers wound bacteria counts. VAC also exerts traction on the wound edges

and helps to mechanically close the wound. It may promote the release of growth factors, as well as alterations in growth rates based on cytoskeletal signals, and it improves the formation of granulation tissue. The VAC dressing has been used on a variety of both acute and chronic wounds and incisions. It can be used on open fracture wounds after irrigation and débridement, open wounds resulting from fasciotomy, infected wounds after adequate débridement, surgical incisions that cannot be closed without tension, and closed surgical incisions with continued wound drainage. Use of a VAC dressing may encourage granulation and lessen the need for grafts or flaps.

It should be noted that VAC is not a substitute for adequate débridement. The VAC dressing should not be used over exposed vascular structures and should be changed at approximately 48-hour intervals as a clean bedside procedure. If the VAC dressing is left in place longer than 48 hours, granulation tissue will grow into the sponge and may require surgical débridement, particularly in younger patients.

Definitive wound coverage or closure of the soft-tissue wound and open tibial fracture should be done within 1 week if possible. The goals of soft-tissue reconstruction of the lower extremity are to achieve a closed and stable wound, avoid infection, enhance bone healing, restore ambulation, and provide improved aesthetics.¹⁵ The hierarchy of traumatic wound closures includes primary closure, delayed primary closure, skin grafting, local flaps, free flaps, and healing by secondary intention. The selection of the appropriate method is based on the mechanism of injury, the location of the injury, the size and shape of the

wound, contamination, and various comorbid factors related to the host.

Primary closure is most appropriate in clean and uncomplicated wounds with minimal tissue injury or loss and small wounds with no gross contamination. Delayed primary closure may be appropriate in situations where there is devitalization of the tissue requiring débridement, a contaminated wound that can be cleaned, or an unclear zone of injury. It may be useful after a fasciotomy. When planning a delayed primary closure, tissue expanders or stretchers can be considered.

Split-thickness skin grafting is appropriate on wounds that are missing skin and cannot be closed without tension but in which a vascularized bed exists or can be obtained. Skin grafts are not effective over exposed bone, tendon, nerve, or vessel.

Local soft-tissue flaps include fasciocutaneous, muscle, and myocutaneous flaps. Fasciocutaneous flaps or rotation flaps are quite useful and can be done throughout the entire length of the tibia.¹⁶ Local muscle flaps include the gastrocnemius, soleus, tibialis anterior, and extensor digitorum longus flaps.

Free vascularized muscle flaps using muscle taken from the latissimus dorsi, rectus abdominus, or gracilis can cover extensive defects. Composite vascularized tissues taken from the forearm, groin, iliac crest, or fibula sometimes are necessary but require specialized microvascular capabilities.¹⁵

Acute Compartment Syndrome

Tibial fracture is the most common cause of acute compartment syndrome (ACS).¹⁷ ACS may occur as a result of the initial injury or as a consequence of surgical stabilization. Acute restoration of length of

a shortened fracture by external fixation or tibial nailing can increase intramuscular pressure (IMP).¹⁸ ACS is considered a surgical emergency, yet it may be difficult to diagnose, and delays in treatment may be associated with significant morbidity. Not surprisingly, a missed or delayed diagnosis of ACS is a common reason for litigation against physicians.¹⁹ This fact was highlighted in a report of the examination of closed claims against physicians for errors in the management of ACS, in which an increasing time from the onset of symptoms to fasciotomy was linearly associated with an increased indemnity payment ($P < 0.05$). In contrast, a fasciotomy done within 8 hours of presentation of symptoms was always associated with a successful defense.²⁰

The initial diagnosis and emergent management of ACS in a patient with a tibial fracture is discussed in this section; the pathophysiology of ACS is covered in more comprehensive studies.²¹⁻²⁴

Clinical Diagnosis

ACS typically is diagnosed using clinical criteria. So-called classic symptoms of ACS are known as the “five P’s”: pain, pallor, pulselessness, paresthesia, and paralysis. However, only escalating pain, pain with passive stretch of the involved muscle, and numbness are realistically useful clinical criteria. Unfortunately, these criteria are extremely subjective, are easily attributed to the associated fracture, may be readily masked by pain medication, and usually are difficult to assess in a splinted limb. Pain with muscle stretch may be caused by direct muscle trauma and may not be a sign of muscle ischemia. The use of regional anesthetic blockade in patients with compartment syndrome should be

avoided, and even routine patient-controlled anesthesia can completely mask the changes in pain intensity that occur with ACS.²⁵ Because peripheral nerves are very sensitive to ischemia, hypoesthesia in a specific nerve located within the involved compartment is a sensitive early finding^{24,26} (Table 3). However, neurologic deficits also may be traumatic and are therefore not specific to compartment syndrome. Specific subsets of patients with ACS, such as those with schizophrenia,²⁷ patients receiving parenteral narcotics or regional anesthesia, or those who are obtunded or intoxicated might not demonstrate significant pain.

The inconsistency and variability in clinical signs and symptoms of ACS decrease the accuracy of clinical diagnosis; therefore, a high index of suspicion must be maintained when caring for patients at risk of ACS. Furthermore, because all patients in whom ACS is diagnosed are treated by fasciotomy, it is impossible to know the rate of false-positive examinations. Ulmer²⁸ reviewed the literature reporting the diagnosis of ACS of the lower leg and found that the sensitivity and positive predictive value of clinical findings for ACS were very low (< 19%). In contrast, the specificity and negative predictive value were each 97% and 98%, respectively. Therefore, the clinical findings associated with ACS of the lower leg are more useful for excluding the diagnosis by their absence than they are in confirming the diagnosis when present.²⁸

Measurement of Intramuscular Pressure

Whenever there is any uncertainty regarding the clinical diagnosis of ACS, IMP measurement should be

Table 3
Potential Sensory Findings Related to Specific Peripheral Nerve Involvement in Patients With Possible Compartment Syndrome of the Leg

Compartment	Specific Peripheral Nerve	Region of Hypoesthesia
Anterior	Deep peroneal nerve	First web space
Lateral	Superficial peroneal nerve	Dorsum of foot
Superficial posterior	Sural nerve	Lateral foot
Deep posterior	Tibial nerve	Plantar aspect of foot

considered. Typically, pressures are measured in the anterior, lateral, and deep posterior compartments using either a commercially available device such as the Intracompartmental Pressure Monitor System (Stryker, Kalamazoo, MI) or an arterial line manometer. Both techniques have acceptable accuracy.²⁹ Unfortunately, interpreting IMP is controversial because there is no uniform agreement on what pressures should be used to indicate the need for fasciotomy.³⁰⁻³² There is wide variation in IMP among patients with tibial fractures, and IMPs that exceed 30 mm Hg can develop in many patients without compartment syndrome.³³ In addition, there are likely to be individual variations in the tolerance of muscle to ischemia, so the significance of a given pressure for a specific patient is not certain.^{34,35} IMPs vary within a single compartment, with statistically significant differences at distances as close as 5 cm from the site at which the highest pressure was recorded.³⁶ IMPs also have been shown to be influenced by the position of the adjacent joints.³⁷ If multiple pressure measurements are made at different locations, there is no certainty as to which measurement is most indicative of the underlying pathophysiology. The most consistent and well-supported threshold for fasciotomy appears to be an IMP within 30 mm Hg of the patient's diastolic blood

pressure.³⁸⁻⁴⁰ This is known as the perfusion pressure (ΔP , or delta P) and is calculated as $\Delta P = \text{diastolic blood pressure} - \text{IMP}$. When ΔP is greater than 30 mm Hg, compartment syndrome is not usually thought to be present; conversely, when ΔP is less than 30 mm Hg for a sustained period of time, a fasciotomy may be necessary. Other criteria for ΔP also have been reported.⁴¹

To further improve the diagnosis of compartment syndrome, as well as to eliminate the inconvenience of having to perform multiple IMP measurements, some experts perform continuous IMP monitoring.^{39,42} McQueen and associates³⁹ have demonstrated that the continuous monitoring of the anterior compartment pressure of a cohort of patients with tibial fractures led to a marked reduction in the incidence of fasciotomy without any apparently missed compartment syndromes. Moreover, when compartment syndrome occurred, it was diagnosed earlier, and those patients who had continuous monitoring also had improved clinical outcomes with fewer healing complications.³⁹ Prayson and associates³³ reported that 53% of patients in their series had at least one IMP measurement that was within 40 mm Hg of their mean arterial pressure (an alternative definition of a borderline perfusion pressure), yet none had signs of or developed sequelae of compartment syndrome. Thus, a sustained trend

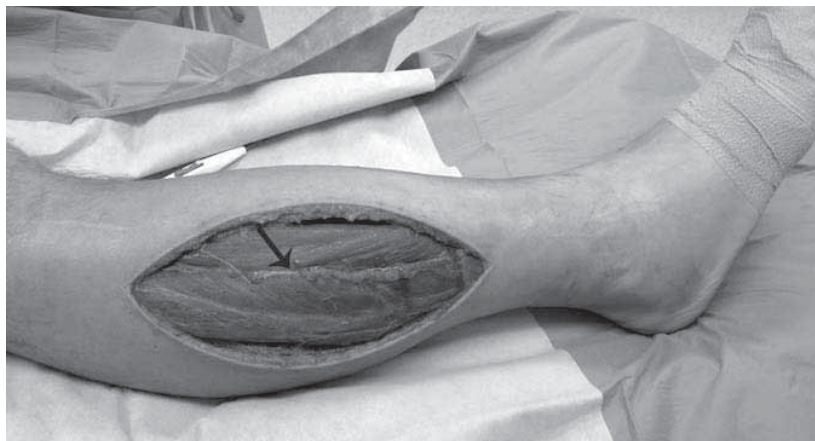


Figure 1 Photograph of the lower leg showing a lateral fasciotomy wound decompressing the anterior and lateral compartments. The lateral intermuscular septum that defines the border between these two compartments is shown (arrow).

of elevated pressures (or inadequate perfusion pressure) is a better indicator of the need for fasciotomy than a single pressure alone. These are strong arguments in favor of continuous monitoring of the anterior compartment (the sentinel compartment) in at-risk patients, but many clinicians still rely primarily on changes in the clinical examination and advocate a low threshold for performing a fasciotomy.

Another area of clinical uncertainty has been the calculation of ΔP in patients who are under anesthesia. The calculated ΔP is influenced by two factors: the patient's blood pressure and the measured IMP. While a patient is under anesthesia, diastolic blood pressure may be artificially low, leading to a similarly low ΔP calculation. Kakar and associates⁴³ recorded blood pressures in a series of patients undergoing tibial nailing. Diastolic blood pressures were lower during surgery than either before or after surgery. However, postoperative diastolic blood pressure was predicted by preoperative blood pressure. Therefore, for an accurate estimation of what a pa-

tient's perfusion pressure will be once he or she is no longer under anesthesia, the preoperative blood pressure can be used. The only caveat to this consideration would be if the patient were going to remain under anesthesia for some period of time. In that circumstance, the intraoperative blood pressure should be used.

Surgical Treatment

Once identified, ACS must be treated by prompt fasciotomy. A longitudinal incision in the skin and fascia that spans the length of the involved compartment allows the muscles to swell out of their restricting fascial envelope, resulting in decompression of the compartment contents and restoration of perfusion to viable tissue. The outcomes for early fasciotomy have been satisfactory.⁴⁴ Some authors recommend the liberal use of fasciotomy as a prophylaxis against ACS.⁴⁵ However, there are several potential complications associated with fasciotomy, including scarring, a prolonged hospital stay, additional surgery to close the wound, increased risk of infection,

measurable impairment of calf muscle function, and possible chronic venous insufficiency.^{30,46-48}

The ability of fasciotomy to prevent muscle and nerve tissue damage depends on a correct and timely diagnosis. Early diagnosis of compartment syndrome and prompt fasciotomy have been shown to lead to more rapid union and improved function in patients with tibial fractures.^{38,39} In contrast, if fasciotomy is done late, the procedure may have little benefit, and delayed fasciotomy may actually be harmful.⁴⁹ Fasciotomy done after myonecrosis has occurred only serves to expose necrotic tissue to potential bacterial colonization and possible infection. Finkelstein and associates⁴⁹ reviewed five patients with delayed diagnosis of compartment syndrome who had fasciotomy performed more than 35 hours after their injury. Of these five patients, one died of multiorgan failure and the others required limb amputation.

Fasciotomy must be done through generous skin incisions with release of all constricting tissues (Figure 1). The precise incisions to be made and the structures that require release vary depending on the specific case. Subcutaneous fasciotomy is not appropriate for ACS.⁵⁰

Two-Incision Leg Fasciotomy

Fasciotomy of the leg is safely and easily done using two incisions: medial and lateral. The two-incision technique is preferred in most instances because it facilitates release of all involved compartments and is familiar to most surgeons. Two incisions are used because it is simpler (and safer) to release the deep posterior compartment of the leg from the medial side. The anterior and lateral compartments are separately released through a lateral incision.

The superficial posterior compartment may be released from either incision. One of the two incisions, typically the lateral one, must span the length of the compartment to ensure adequate release of the skin. Inadequate skin incisions contribute to persistent elevation of IMP.⁵¹ When a two-incision technique is used, the intervening skin flap may be at risk of necrosis if there has been damage to the anterior tibial artery. If anterior tibial artery injury is recognized before surgery, a single incision, four-compartment release from a lateral approach may be more appropriate (see next section).

First, a lateral incision is made at or anterior to the mid-lateral axis of the leg, midway between the fibula and anterior crest of the tibia. Skin flaps are sharply elevated both anteriorly and posteriorly, exposing the fascia of the anterior and lateral compartments. The fascia over the peroneal muscles usually is released first. The lateral intermuscular septum that divides the anterior and lateral compartments and the superficial peroneal nerve are identified. Finally, the fascia over the anterior compartment is completely released. Alternatively, the fascia overlying one compartment can be released followed by division of the intermuscular septum to decompress the other compartment. However, iatrogenic injury to the superficial peroneal nerve may be more likely with this technique.³⁵

Next, a medial incision is made 1 cm behind the posteromedial border of the tibia. The saphenous vein and nerve should be identified. The fascia of the gastrocnemius-soleus complex should be completely released. Proximally, the soleus bridge should be released to identify and decompress the proximal portions of the flexor digitorum longus and

posterior tibialis muscles. These components of the deep compartment also should be completely released.

Single-Incision Leg Fasciotomy

Fasciotomy of the leg can be done through a single lateral incision, extending from the neck of the fibula to the lateral malleolus. Fibulectomy is no longer considered necessary.³⁵ The anterior and lateral compartments are released in the same manner described for two-incision fasciotomy. The superficial posterior compartment, consisting of the gastrocnemius-soleus complex, is easily released by elevating the skin posteriorly. A parafibular approach is used to decompress the deep posterior compartments of the leg. The peroneal muscles are retracted anteriorly, and the dissection is carried posterior to the fibula. With the lateral head of the gastrocnemius and soleus retracted posteriorly, the septum dividing the superficial and deep posterior compartments can be identified and released. If access to the deep posterior compartment is difficult, a medial incision can be made as previously described.

Management of Fasciotomy Wounds

Several methods can be used to manage a wound following a fasciotomy. Traditionally, fasciotomy wounds are covered with sterile, moist gauze until they are ready for delayed closure or skin grafting. Fasciotomy closure before 5 days is not recommended and can be associated with recurrent compartment syndrome.⁵² Skin grafting is associated with fewer complications than either primary or delayed wound closure.⁵³ Dermatraction using simple vessel loops, prepositioned sutures, or commercially available devices may allow delayed wound closure with-

out surgery or risk of recurrent compartment syndrome.^{54,55} A more recent advance in the management of fasciotomy wounds is the Wound V.A.C. device (KCI USA, Inc, San Antonio, TX). When applied at the time of fasciotomy, the Wound V.A.C. device may allow earlier fasciotomy closure and decrease the need for skin grafting. Clinical results of fasciotomy management with the Wound V.A.C. device have not yet been published.

Acute Infection After Surgical Stabilization of the Tibia

Acute postoperative infection following the surgical stabilization of a tibial fracture is a complication that can threaten the ability to obtain fracture healing and to successfully salvage the injured limb. Concepts on the pathophysiology of implant-associated infection can be used to formulate a rational approach for the management of this condition.

Pathophysiology of Infections After Surgical Stabilization of the Tibia

Bacterial Virulence Factors

Bacteria rapidly colonize open wounds, whether traumatic in origin or occurring during surgical repair of a closed fracture. In particular, the surface of standard metal implants is electrochemically active, providing a surface that can promote adhesion of either host proteins or bacteria. The fact that the same surface is available for both bacterial and eukaryotic (host) cell adhesion is what prompted Gristina to describe the initial events following placement of orthopaedic implants as “the race for the surface.”⁵⁶ Metal surfaces in vivo are rapidly covered with proteins. In turn, bacteria may be attracted to the same surface by nutrients concentrated at implant

surfaces. Many pathogenic species of bacteria are stimulated by the adhesion process to proliferate and to excrete a polysaccharide coating, which is known as a biofilm. Studies have shown that species of *S aureus* retrieved from clinical infections express specific cell surface adhesions or receptors for host proteins, such as bone sialoprotein and fibronectin.⁵⁷

Biofilms contribute greatly to the difficulty in treating biomaterial-associated infections. Biofilms are highly ordered, three-dimensional mucopolysaccharide structures with aqueous channels that provide for the diffusion of nutrients as well as signaling molecules. In fact, bacteria within a biofilm exhibit behaviors not possible when they are in their planktonic (nonadherent) state. For example, it is recognized that adherent *Staphylococcus* organisms are more resistant to antibiotics than the same strains grown in a nonadhered state.⁵⁸ Bacteria survive within biofilms even when exposed to antibiotic levels that are 100- to 1,000-fold greater than their minimal inhibitory concentration in vitro.⁵⁹ Even sensitive bacteria may exhibit reduced sensitivity to a given antibiotic when in a biofilm.⁶⁰

A relatively recent discovery is the way that bacteria within a biofilm communicate with each other through a process that has been termed quorum sensing.⁶¹ It was noticed that bacteria within biofilms exhibit behaviors that are unproductive when undertaken by an individual bacterium but become effective by the concerted action of a group of cells. Such behaviors include bioluminescence, the expression of virulence factors, and biofilm formation. It has been shown that quorum sensing is achieved through the production, release, and subsequent de-

tection of and response to threshold concentrations of signal molecules called autoinducers.

Another important virulence factor for *S aureus* is its ability to exist intracellularly within macrophages.⁶² In one study, in which macrophages were cocultured with *S aureus*, the macrophages were shown to ingest the staphylococcal organisms, which survived within the macrophage and its eventual cell death. Upon cell lysis, viable *S aureus* organisms were released and were shown to be capable of reinfecting another cell.⁶² Furthermore, the intracellular *S aureus* organisms rapidly became resistant to bacteriostatic antimicrobial agents, and the development of resistance was associated with the development of a thick cell capsule visible with electron microscopy.

Immunomodulation

Notable alterations of immunologic function are seen in the local environment about metal implants. These include impaired polymorphonuclear cell function, T cell inhibition, plasma cell activation, changes in cytokine concentrations, and decreased immunoglobulin production. Although the clinical significance of these factors is not known, such changes may impair the host response to biomaterial-associated infection.

The Role of Fracture Stability

It is known that the presence of a foreign body increases the risk of infection, yet clinical experience suggests that internal fixation of open fractures reduces the infection rate. This apparent conflict creates a real dilemma for clinicians who must decide whether or not to remove an infected implant. In the case of a healed fracture, hardware removal is

simple and often is all that is necessary to resolve the infection. However, when there is a fresh fracture with acute infection, removal of hardware may be counterproductive because of fracture instability.

In one study using a rabbit model, tibial fractures were stabilized with either a stable dynamic compression plate or an unstable intramedullary rod. Animals in both groups were inoculated with *S aureus*. The infection rate was double in the unstable group (71% versus 35%).⁶³ The mechanisms by which stable fracture fixation reduces the rate of infection are not exactly understood, but it is thought that stable internal fixation reduces ongoing soft-tissue damage caused by fracture instability and promotes more rapid vascular invasion and restoration of the microcirculation, all of which make the wound a less hospitable environment for bacterial growth.

Diagnosis of Infection After Surgical Stabilization of the Tibia

An infected fracture may be the cause of persistent pain, prolonged wound drainage, or delayed union of a fracture treated with internal fixation. With respect to infection occurring after tibial nailing, Court-Brown and associates⁶⁴ described three presentations: (1) fever with localized pain, swelling, and erythema at the fracture site without abscess formation; (2) obvious purulence at the fracture site; and (3) delayed presentation with purulent drainage from the fracture site.

When a fracture is possibly infected, laboratory studies are of uncertain value, other than a confirmatory positive culture. Sepsis usually is accompanied by elevations in total leukocyte count, erythrocyte sedi-

mentation rate (ESR), or C-reactive protein (CRP). However, in the subset of patients in whom infection occurs soon after a traumatic event and subsequent surgery, these same parameters are likely to be elevated even in the absence of infection, making their measurement of less value. In the total joint literature, a rising CRP after 48 hours is predictive of a septic complication.⁶⁵ In a study of 330 patients who had surgical fracture treatment and who had preoperative and at least three postoperative CRP levels measured, the peak value occurred on the second postoperative day.⁶⁶ The magnitude of CRP elevation was proportional to the degree of surgical trauma, and patients with complications had a second rise in their CRP level. In this study, seven of nine patients with infections had increasing CRP levels before the onset of clinical symptoms.⁶⁶ Therefore, serial measurement of CRP in the postoperative fracture may be of clinical value.

Imaging studies generally are nonspecific in an acute infection. Classic radiographic findings seen in chronic infections, such as reactive or periosteal new bone formation, demineralization, or a sequestrum, are not present in early infections. Indium-labeled white blood cell scans and MRI may also be useful, but infrequently are diagnostic.

The most accurate indicator of infection is the finding of bacteria on Gram stain or culture. However, in the setting of a biomaterial-associated infection, even bacterial culture may be associated with falsely negative findings. It has been shown that sonication of implant surfaces dislodges adherent bacteria and increases yield fivefold.⁶⁷ Furthermore, examination of sonicated samples by immunofluorescence microscopy and polymerase chain

reaction increased yield tenfold.⁶⁸ Neut and associates⁶⁹ studied 22 suspected infections in patients with prostheses and found that routine cultures of swabs or tissue specimens were positive in 41%, while prolonged culturing produced positive cultures in 64% and extensive culturing of scrapings from implant surfaces led to positive findings in 86%.

Treatment of Infections After Surgical Stabilization of the Tibia

When caring for an infected fracture, there are two basic approaches: (1) obtain fracture union first and then deal with the infection or (2) treat the infection first and then deal with the ununited fracture. The first option usually entails maintenance or one-stage replacement of the existing internal fixation, whereas the second option encompasses implant removal and, typically, conversion to external fixation. The first option is appropriate in fractures with stable internal fixation and when fracture union appears to be progressing despite the infection. Specific management tactics that fall in this category might include medical management with antibiotic therapy alone; débridement with implant retention; or immediate implant removal, débridement, and replacement. When the fixation is unstable, or the wound cannot be rendered sterile despite repeat débridements, then implant removal with delayed reimplantation or conversion to alternative fixation likely is necessary.

Deciding whether or not implant retention is appropriate depends on many factors and demands careful clinical judgment. Factors to consider include the health of the host, the extent of bone healing that has occurred, the viability of the soft-tissue envelope, the duration of clinical symp-

toms, the infecting organism(s), and the nature of the associated implant.

Infections that occur after fracture union are the simplest to treat and typically are managed by local débridement, implant removal, and a relatively short course (2 to 4 weeks) of appropriate antibiotic therapy, which may be either parenteral or oral depending on the organism and its sensitivity to antibiotics.

Infections that develop before fracture healing are much more difficult to treat because the issue of limb stability also must be considered. Thus, for an ununited fracture, treatment depends on maintaining bone stability, but this must be balanced against the possible need to remove all colonized hardware. Simply removing the implant, as can be done after fracture healing, will leave the patient with an unstable fracture. Fortunately, in the case of a tibial fracture, the limb may be stabilized adequately in a cast or external fixator; either can be used for definitive management if needed.

In one of the few reports of protocol-directed treatment, Hofmann and associates⁷⁰ reported their experience with 34 patients who had acute infections following internal fixation. The goal of these authors was to eradicate the infection and avoid the development of chronic osteitis, while maintaining the existing internal fixation, if possible. The authors' surgical protocol was to perform repeated surgical irrigation and débridement every 2 days, up to four times. If the surgical site was not bacteriologically sterile after four débridements, the implant was removed. The implant was successfully maintained, and the infection eradicated in 11 of the 34 patients (32%). In 23 patients (68%), the implant material had to be removed. These investigators found that im-

plant removal was required in every patient who had diabetes or arteriosclerosis or used alcohol or nicotine.⁷⁰

Bone Loss

Many open tibial fractures are characterized by bone loss, or large bone fragments are removed at the time of the initial débridement. Except for small defects (less than one third of the diameter of the tibia and less than 1 cm in length), virtually all tibial shaft defects will require some sort of bone reconstruction. Although spontaneous healing of large tibial defects has been reported,⁷¹ this is the exception rather than the rule for the tibia, and a plan for management of any bone loss must be part of the overall surgical tactic.

Management of tibial bone loss depends on the amount of bone loss and the status of the overlying soft tissues. As a general rule, defects less than 4 cm can be easily managed with simple bone grafting, whereas defects larger than 4 cm may require some other form of treatment, such as bone transport. This somewhat arbitrary limit is determined primarily by the amount of autologous bone that can be harvested from the iliac crest. It has also been generally accepted that bone grafting in the tibia should be delayed.⁷² However, the recent introduction of recombinant bone morphogenetic proteins (BMPs) has challenged traditional concepts about the timing of bone grafting and the size of the defect for which bone grafting is indicated.⁷³

Review of Fracture Healing

It is now known that fracture healing requires the concerted interaction of collagen matrix, noncollagen proteins (growth factors), and bone-forming cells. Materials thought to promote fracture healing are charac-

terized by their ability to replicate one or more of these properties. Osteoconductive materials contain collagen or other materials that can be used to regenerate a scaffold for bone formation. Most bone graft substitutes are osteoconductive. Osteoinductive materials represent a source of growth factors that stimulate the recruitment and differentiation of bone-forming precursor cells into osteoblasts. Osteogenic materials contain a source of bone-forming (or precursor) cells that are capable of responding to appropriate stimuli and initiate bone formation. Only recently have bone graft substitutes with any significant osteoinductive or osteogenic potential become available.

Management of Large Defects (> 4 cm)

The gold standard for bone grafting of small defects has been autogenous iliac crest graft. The use of autologous bone graft for larger defects is limited by the amount of bone that can be harvested as well as morbidity associated with obtaining bone graft from the iliac crest.⁷⁴ Therefore, treatment of large long bone defects has usually required alternative approaches such as bone transport, vascularized fibula grafting, or acute shortening followed by later lengthening. More recently, techniques to harvest bone graft from the medullary canal of the femur (RIA, Reamer Irrigator Aspirator; Synthes USA, Paoli, PA) have been developed and represent a less invasive way to obtain larger quantities of bone.⁷⁵ Interestingly, bone graft from the femur has been shown to contain both viable stem cells⁷⁶ and higher quantities of growth factors than bone obtained from the iliac crest,⁷⁷ although the clinical significance of this is unknown. Using bone ob-

tained from the femur with the RIA, McCall and associates (unpublished data presented at the Orthopaedic Trauma Association annual meeting, Boston, MA, October 2007) successfully grafted segmental bone defects up to 14.5 cm in length.

In 2004, recombinant human BMP-2 (rhBMP-2) was approved by the FDA for use in open tibial fractures thought to be at risk for healing complications. Jones and associates⁷³ recently reported a series of 30 adult patients with tibial shaft defects following the treatment of open fractures. At the time of staged bone grafting at a mean of 11 weeks postinjury, patients were randomly assigned to receive either autogenous bone graft or cancellous allograft augmented with an onlay strip of rhBMP-2 on an absorbable collagen sponge. Ten of 15 patients in the autograft group and 13 of 15 patients in the rhBMP-2/allograft group healed without further intervention.⁷³

The timing of bone grafting of the tibia has been a source of controversy. Fischer and associates⁷² found that patients with tibial fractures and severe soft-tissue injury who underwent delayed bone grafting after wound reepithelialization had fewer infections and more rapid union. Recent studies in which fractures were grafted with rhBMP-2 have indicated that early bone grafting may be possible. Murnaghan and associates⁷⁸ used a mouse femoral fracture model to show that healing of a critical defect was better after immediate or early grafting than after later grafting. In another investigation, Makino and associates⁷⁹ studied femoral nonunion in a rat model. A closed fracture was created and stabilized with a retrograde pin. The fracture site was then opened, and the periosteum was cauterized on

each side of the fracture. One group of animals had the site grafted with BMP-7, while the control group was grafted with collagen alone. None of the control femoral fractures healed, whereas all of the BMP-treated bones were healed within 6 weeks. The authors concluded that the early application of BMP-7 can rescue the fracture healing process and prevent nonunion in fractures associated with periosteal disruption.⁷⁹

These investigations suggest that BMPs may extend or replace the use of autograft and may allow immediate rather than delayed bone grafting. Further research is necessary before definitive recommendations can be made.

New Approaches to Treating Bone Loss

Cell-Based Approaches

Although it has been recognized for some time that cells are responsible for much of the osteogenic capacity of autograft bone,⁸⁰ only recently has there been widespread interest in cell-based approaches to bone grafting. Stem cells capable of transforming into osteoblasts exist in many tissues, including bone marrow, adipose tissue, and the vascular pericyte. It is now possible to create a “cocktail” of osteoconductive materials, osteoinductive growth factors, and osteogenic cells that would seem to reconstitute nearly all of the components of autologous bone marrow. Bruder and associates⁸¹ created blocks consisting of 65% hydroxyapatite and 35% β -tricalcium phosphate, cut into cylinders 14 mm in diameter with an 8-mm central canal. Some of the implants were coated with human fibronectin, loaded with cells, and incubated. Canine femoral defects were implanted with either the cell-loaded implants or barren implants. Frac-

ture healing was far more robust in the animals that received the implants loaded with cells.⁸¹

Titanium Cage

A novel approach to the reconstruction of large defects of the tibia has been described by Cobos and associates⁸² and Attias and Lindsey.⁸³ Attias and Lindsey reported three patients with severe tibial fractures associated with extensive segmental bone and soft-tissue loss (mean bone defect size, 12.2 cm). After initial serial wound débridement and external fixation, the soft-tissue defects were reconstructed. After maturation of the soft-tissue flaps, the external fixator was removed, and the bone defects were reconstructed using a cylindrical titanium mesh cage that was filled with a mixture of cancellous allograft and demineralized bone matrix putty and stabilized with a statically locked nail. One year after reconstruction, follow-up radiographs showed stable, well-aligned, healed constructs. CT images verified the presence of bony ingrowth throughout the cages, and all three patients were able to bear full weight.

Induced Membrane: Masquelet Approach

In 2000, Masquelet and associates⁸⁴ reported in the French literature a series of 35 patients with large diaphyseal defects that were reconstructed in two stages using a technique that has since been described as membrane-guided bone regeneration. In the first stage, the residual bone defect was filled with PMMA, and the soft tissue was closed. During the following weeks, the PMMA spacer became surrounded by a pseudosynovial membrane. At the second stage, the PMMA spacer was removed, with care not to disrupt

the surrounding membrane. The remaining contained cavity was then filled with autogenous bone graft. Important technical points are that the spacer should envelope the ends of the bone above and below the defect, and the medullary canal should be opened at the time of the bone grafting. It has been subsequently shown that the induced membrane contains both vascular and osteoinductive growth factors, including BMP-2, that can promote bone formation.⁸⁵

Summary

Advances in intramedullary nailing and the use of statically locked intramedullary nails have provided a near universal means of fixation for displaced open tibial shaft fractures. However, infections, compartment syndromes, and bone loss are common complications that continue to complicate the early treatment of open tibial fractures. A better understanding of the basic science of infection, débridement, and irrigation of open fractures will help to reduce rates of infection. Compartment syndromes continue to be a complication of both diagnosis and management. Despite a high index of suspicion, compartment syndromes will continue to occur, and therefore better means of monitoring are needed for treatment in the future. Significant developments in the availability of bone graft substitutes and biologic mediators to enhance bone formation offer great hope in managing bone loss and securing earlier and improved rates of union.

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