

Medical Student Research Project

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Acute Management of Open Long Bone Fractures: Clinical Practice Guidelines

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Abstract

Introduction: The acute management of an open fracture aims to promote bone and wound healing through a series of key steps; however, lack of standardization in these steps prior to definitive treatment may contribute to complications.

Methods: A literature review was conducted to determine the best practice in the acute management of open long bone fractures to be implemented at Temple University Hospital, with a primary focus on prophylactic antibiotic administration, local antibiotic delivery, time to debridement and irrigation techniques.

Results: A computerized search yielded 2,037 results, of which a total of 21 articles were isolated and reviewed based on the study criteria. The final total was then subdivided into the topics focused on in this review: duration of prophylactic antibiotics (n = 2), local antibiotic delivery (n = 7), time to debridement (n = 10), and irrigation techniques (n = 2).

Conclusion: Recommendations were developed based on a review of clinical studies on open fracture management. Prophylactic antibiotic recommendations, including coverage of choice and duration of administration, were adapted from the guidelines proposed by the Eastern Association for the Surgery of Trauma workgroup. In addition, the use of local antibiotic delivery techniques may prove beneficial as an adjunct to systemic prophylactic antibiotic therapy in the management of severe open fractures and in patient populations where prolonged antibiotic therapy is otherwise indicated. Debridement and irrigation should occur emergently, but only if resources are available. A low-pressure (6–10 pounds per square inch) lavage system using either detergent or saline, with increased volumes for more severe fractures, is recommended prior to fracture fixation to reduce the bacterial load.

Introduction

Current complications of an open fracture include infection, nonunion of the fracture, and missed compartment

syndrome,^{1,2} often resulting in loss of function of the limb. Infection rates can range from 0–50% depending on fracture severity and location^{2–5} and nonunion rates are reported at an incidence of 18–29%.^{6,7} Historically, amputation of the fractured limb and mortality were commonly associated with open fractures.^{8,9} However, due to developments in its management, outcomes for open fractures have generally improved, as limbs are often salvaged and patients can retain function of the injured extremity. Despite generalized standards for open fracture treatment, there remains variation and controversy over the initial management of open fractures, which may contribute to complications following treatment.

Open fractures occur when the fractured bone penetrates through the skin, involving damage to the bone and soft tissue. Complications following an open fracture relate to the severity of soft tissue injury,³ which became the basis of the open fracture classification system as described by Gustilo and Anderson. Despite recent reports of interobserver variability in fracture classification,¹⁰ the Gustilo-Anderson classification of open fractures has been used for many years. In 1976, open fractures were divided into three categories (Table 1). Type I fractures were described as open fractures that resulted in a laceration length of less than one centimeter, were moderately clean and had minimal soft tissue injury. Type II fractures were wounds greater than one centimeter in length with moderate soft tissue damage. Type III fractures had extensive soft tissue damage and a high degree of contamination.³ Several years later, Type III fractures were further divided: Type IIIa fractures had adequate soft tissue for bone coverage; Type IIIb involve loss of soft tissue, including periosteal stripping; and Type IIIc involve arterial injury requiring repair.¹¹ These fracture classifications are currently used in practice to determine the appropriate steps in the treatment of an open fracture.

The management of open fractures includes adherence to Advanced Trauma Life Support (ATLS) guidelines, assessment of neurovascular injury, prophylactic antibiotic and tetanus toxoid administration within three hours of injury,^{1,12–14} temporary coverage of the wound with sterile saline soaked gauze, emergent meticulous debridement and irrigation,

temporary or definitive fixation, and wound closure and coverage,^{1,7,15-17} with the latter operative steps commonly left to the discretion of the surgeon. Goals of treatment focus on bone and wound healing, with the prevention of infection.^{8,18} The lack of agreement over key steps in the initial management of open fractures may contribute to common complications such as infection or nonunion of the fracture.

Recent guidelines have described prophylactic antibiotic use in the management of open fractures based on fracture classification (Table 1, Appendix 1a and 1b).^{9,13,14} Nonetheless, noncompliance with these recommendations occurs, such as antibiotic use exceeding the recommended duration, which can lead to further complications.¹⁹ Additional concerns with prolonged antibiotics use are the development of antibiotic resistance, allergic reactions, host toxicity and increased costs.^{9,17} Several studies evaluate the benefits of local antibiotic delivery as adjunctive prophylactic therapy in the management of open fractures in an effort to decrease systemic levels of antibiotic.^{16,20-27}

Another area of current debate is the urgency of surgical intervention, from the time of injury to initial debridement. The “six-hour” window for operative treatment, which has been the standard practice in the management of open fractures for several decades, is being reevaluated to assess the scientific validity of such a timeframe and whether operative treatment within this time period is advantageous to the patient. Recent studies have suggested that the experience and preparedness of the surgical team may be a more important determinant in treatment outcome²⁸ and that a delay in operative treatment until the appropriate resources are available may reduce the risk of poor outcomes.^{6,29}

Irrigation is another critical step in the initial management of an open fracture, as it serves to reduce the bacterial load in the wound.^{30,31} However, there remains great variation in the techniques used for irrigation of the wound,³² some of which may result in complications, including poor wound healing, delay in fracture healing, host toxicity and the increased risk of infection.^{30,33-37}

The purpose of this study is to conduct a literature review to develop current recommendations for the initial manage-

ment of open fractures in long bones to be implemented at Temple University Hospital (TUH), with a primary focus on prophylactic antibiotic administration, local antibiotic delivery, time to debridement, and irrigation techniques, and assess how these influence the development of complications seen commonly after the treatment of an open fracture.

Methods

A literature review was conducted by a computerized search using the MEDLINE database with the following medical subject headings (MeSH) terms: *Fractures, Open* [Mesh] AND *Fractures, Open/classification* [Mesh] AND *Fractures, Open/therapy* [Mesh]; *Fractures, Open* [Mesh] AND *Antibiotic Prophylaxis* [Mesh] AND *Antibiotic Prophylaxis/adverse effects* [Mesh]; *Fractures, Open* [Mesh] AND *Therapeutic Irrigation* [Mesh]; *Fractures, Open* [Mesh] AND *Surgical Wound Infection* [Mesh]; *Fractures, Open* [Mesh] AND *Debridement* [Mesh]; (*Arm Bones* [Mesh] OR *Leg Bones* [Mesh]) AND *Fractures, Open* [Mesh]; *Antibiotic Prophylaxis* [Mesh] AND *Drug Resistance, Bacterial* [Mesh] AND *Surgical Wound Infection* [Mesh]; *Fractures, Open* [Mesh] AND *Fractures, Open/complications* [Mesh] AND *Therapeutic Irrigation* [Mesh] AND *Surgical Wound Infection; Fractures, Open/complications* [Mesh] AND (*Fractures, Open/surgery* [Mesh] OR *Fractures, Open/therapy* [Mesh]); *Fractures, Open* [Mesh] AND *Anti-Bacterial Agents/administration and dosage* [Mesh]; *Fractures, Open/surgery* [Mesh] AND *Polymethyl Methacrylate* [Mesh]; (*Fractures, Open* [Mesh]) AND *Poly-methyl Methacrylate* [Mesh] AND *Anti-Bacterial Agents* [Mesh]. Additional key words used in the search included *local antibiotic* and *antibiotic bead pouch*.

Through a title and keyword review of the initial search results, studies were considered if they included open fractures of long bones, such as the tibia, femur, humerus, and forearm, in an adult population. Studies were excluded from the review if they did not meet the inclusion criteria, were not published in English, were not performed on human subjects, used a patient population that was younger than 19,

Table 1. Fracture Classifications and Prophylactic Antibiotic Recommendations

Classification	Description	Antibiotic Recommendations
Type I	<1 cm wound, minimal soft tissue damage, moderately clean	First generation cephalosporin (gram-positive coverage), continued for 24 hours after wound closure.
Type II	>1 cm wound, moderate soft tissue damage	First generation cephalosporin (gram-positive coverage), continued for 24 hours after wound closure. The addition of a once-daily aminoglycoside is safe and effective.
Type III	Extensive soft tissue damage, high degree of contamination	First generation cephalosporin (gram-positive coverage) and aminoglycoside (gram-negative coverage) continued for 72 hours after injury, but no more than 24 hours after soft tissue coverage of the wound. Penicillin is recommended for farm-related injuries, with soil or fecal matter contamination. Fluroquinolones offer no advantage over cephalosporins and aminoglycosides and have been found to have a negative impact on open fracture outcome.
Type IIIa	Adequate soft tissue coverage of bone	
Type IIIb	Loss of soft tissue, periosteal stripping	
Type IIIc	Vascular injury needing repair	

Fracture classification as described by Gustilo and Anderson and by Gustilo et al.^{3,11}

Antibiotic recommendations as per the Eastern Association for the Surgery of Trauma (EAST) guidelines proposed in 1998 and 2011.^{13,14}

classified gun shot wounds as open fractures, or contained pelvic bones or long bones of the hand or foot. Papers fit for the study were further isolated through an abstract and article review, excluding studies that did not fit the topic of the current review. In addition, references of relevant review articles were reviewed for citations missed by the initial computerized search, and were subjected to the same review process as described above.

Articles that met the inclusion and exclusion criteria were later subdivided into the topics focused on in this review: prophylactic antibiotic administration, local antibiotic delivery, time to debridement, and irrigation techniques.

Results

Search Results

The initial search yielded 2,037 results, 485 of which were duplicates, resulting in 1,552 articles (Figure 1). Filters were then applied to remove studies that were not published in English, were not performed on human subjects and used a patient population that was younger than 19. Reviews were also removed from consideration, resulting in 640 articles for title review. Four hundred and ninety-one articles were excluded through a title review based on exclusion and inclusion criteria. The resulting articles were subjected to abstract and article reviews resulting in 18 papers. Three articles were added through a review of references of relevant reviews. The final total (n = 21) was then subdivided into the topics focused on in this review: duration of prophylactic antibiotics (n = 2), local antibiotic delivery (n = 7), time to debridement (n = 10), and irrigation techniques (n = 2).

Prophylactic Antibiotic Duration

The database search resulted in one article that met the criteria for the study of prophylactic antibiotic duration in the management of open fractures, and a review of the references of relevant reviews produced an additional study. A total of two articles were reviewed for the study of prophylactic antibiotic duration in the management of open fractures (Table 2).

In an earlier work from 1988, Dellinger and colleagues³⁸ conducted a double blind randomized prospective study comparing the efficacy of a one-day versus a five-day prophylactic antibiotic regimen for the management of open fractures in the arm and leg. This study found no statistical difference in infection rates between patients that received the short duration antibiotic regimen compared to those that received the five-day regimen (27% vs 23%), demonstrating that a short duration of antibiotics is as effective as a longer duration.

More recently, Dunkel et al.³⁹ assessed the risk of infection following varying durations of prophylactic antibiotic treatment in 1,492 open fractures using a retrospective case control model. The odds ratio (OR) for infection based on antibiotic duration using a multivariable regression analysis was

Figure 1. Method of Article Selection for Literature Review

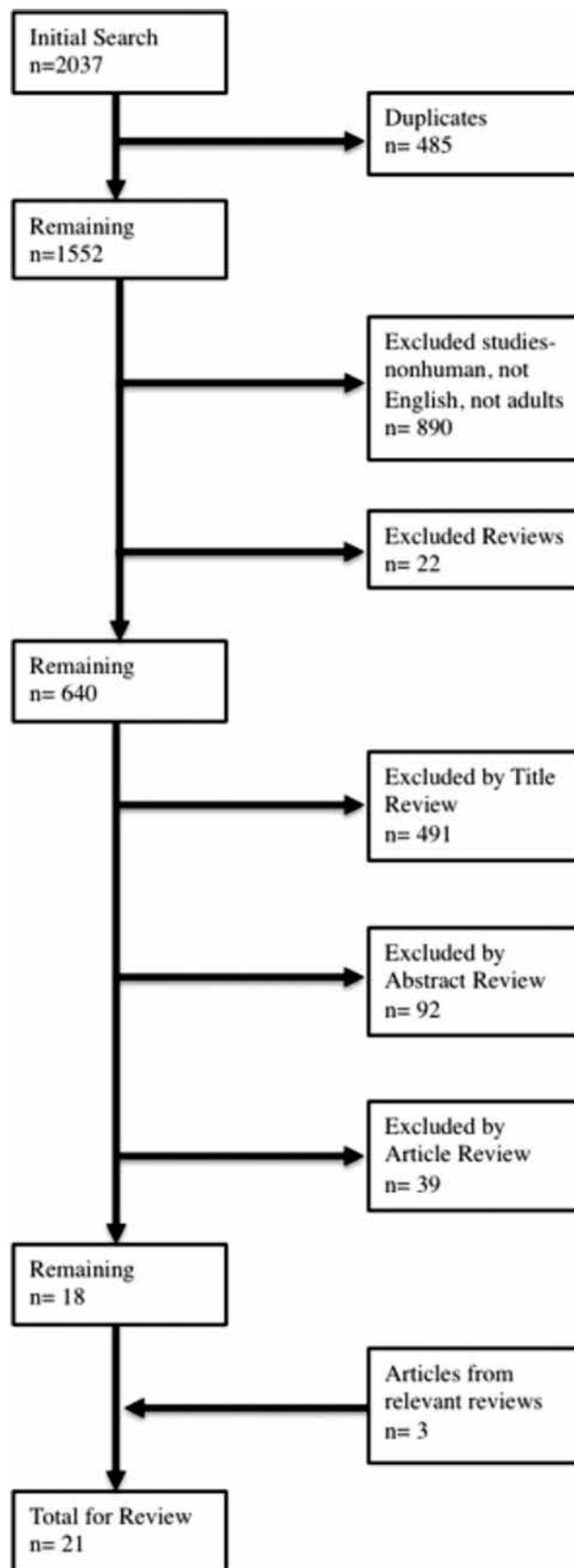


Table 2. Prophylactic Antibiotic Duration — Study Details

Author	Year	Study Design	Results	Conclusions
Dunkel ³⁹	2013	Retrospective case control study; n = 1492; compared varying durations of antibiotic treatment using univariate and multivariable regression analyses	Antibiotic duration groups of 1 day, 2–3 days, 4–5 days, and >5 days were compared. Multivariate OR were reported as follows: 1 day: reference 2–3 days: 0.6 (0.2–2.0) 4–5 days: 1.2 (0.3–4.9) >5 days: 1.4 (0.4–4.4) None were significant. A significant difference (p < 0.001) was found in a univariate analysis in the OR for 4–5 days (8.9) and for >5 days (9.8)	Increased duration of antibiotics is not related to infection
Dellinger ³⁸	1988	Double blind randomized prospective study; 248 patients with open long bone fractures were divided into three treatment groups: (1) 2 g cefonicid sodium IV x 1 day (n = 79) (2) 2 g cefonicid sodium IV, followed by 1 g/24 hours x 5 days (n = 85) (3) 2 g cefamandole nafate IV, followed by 1 g/6 hours x 5 days (n = 84)	Infection rates between the groups had no statistical significance: (1) 27% (2) 23% (3) 27% Fracture site infections were compared between 1-day groups (1) vs 5-day groups (2, 3): 1 day: 13% 5 day: 12%	Short duration of antibiotics is as effective as a longer duration

OR = odds ratio; IV = intravenous

reported: one day, reference; 2–3 days, 0.6 (confidence interval (CI) 0.2–2.0); 4–5 days, 1.2 (CI 0.3–4.9); and >5 days, 1.4 (CI 0.4–4.4), all failing to reach statistical significance. These results show that there was no association between infection and duration of prophylactic antibiotic administration.

Local Antibiotic Delivery

The database search resulted in a total of six studies that met the criteria for the study of local antibiotic delivery in the management of open fractures in adults. An additional study was found through a reference review of relevant review articles resulting in a total of seven articles for consideration in this study (Table 3).

A group from the University of Louisville, Ostermann, Henry and Seligson, conducted a series of five retrospective reviews that contributed greatly to the study of local antibiotic delivery in the management open fractures.^{20, 21, 24-26} In the most recent study, 1,085 consecutive open fractures in 914 patients were analyzed to assess the effects of local antibiotic administration on the incidence of infection. The adjuvant use of local antibiotics using tobramycin-impregnated polymethylmethacrylate (PMMA) beads resulted in a significant decrease in infection rates compared to patients that were administered only intravenous antibiotics prophylactically (3.7% vs 12%). Furthermore, Type IIIb fractures demonstrated a statistically significant decrease in overall infection rates with the adjuvant use of local antibiotics (6.5% vs 20.6%), whereas other fracture grades showed a trend of decreased infection rates, failing to reach statistical significance.²⁵ Earlier studies conducted by the same group had similar outcomes.^{20, 21, 24} Seligson et al.²⁶ reviewed 72 Type IIIc fractures that required vascular repair from the study population described above, 40 of which were treated with tobramycin-impregnated PMMA beads as an adjunct to systemic prophylactic antibiotic therapy. Wound infection rates

significantly decreased with the use of supplemental local antibiotic delivery compared to systemic antibiotic administration alone in the management of severe open fractures (5% vs 25%, respectively).

In 1996, Keating et al.²² treated 81 open Type II and III tibia fractures with reamed intramedullary nailing comparing the effectiveness of a combination of systemic antibiotic administration with a local antibiotic pouch to the use of only systemic antibiotic use in preventing infection. The addition of the antibiotic bead pouch reduced deep infection rates from 16% to 4%. Though decreases were found in infection rates in each fracture classification, none of these were statistically significant.

The most recent clinical study compared the use of local antibiotic delivery to intravenous administration of antibiotics in a pilot randomized prospective study. Moehring et al.²³ randomly divided patients of Type II, IIIa and IIIb open long bone fractures to receive either local antibiotics or systemic antibiotics following surgical intervention. A third cohort was nonrandomly assigned to be co-administered local antibiotic-impregnated beads and intravenous antibiotics. Patients in this third group, however, were treated for either nonorthopaedic reasons or sustained a limb threatening injury. Infection rates of the three groups reported were 8.3%, 5.3% and 15.4%, respectively.

Time to Debridement

The database search resulted in nine citations that met the criteria for the relationship between time to debridement and infection rates in the management of open fractures. The references of recent review articles were searched to find publications missed by the database search resulting in a total of 10 articles for review (Table 4).

In 1989, Patzakis and colleagues⁴ evaluated 1,104 open fractures retrospectively to determine predisposing factors to

Table 3. Local Antibiotic Delivery — Study Details

Author	Year	Study Design	Results	Conclusions
Moehring ²³	2000	Randomized prospective pilot study and a nonrandomized prospective study. n = 75 open long bone fractures. Study groups: Local Antibiotic beads (n = 24) Systemic Antibiotics (n = 38) Systemic and Local, nonrandomized (n = 13)	Infection Rates: Local Antibiotics: 8.3% Systemic Antibiotics: 5.3% Systemic + Local: 15.4% Not statistically significant	Suggests that local antibiotic delivery can be used as an adjunct to systemic antibiotic administration to prevent infection in open fractures
Keating ²²	1996	Retrospective review of 81 Type II and III open tibia fractures treated by reamed intramedullary nailing. Study groups: Systemic Antibiotics (n = 26) Systemic and Local Antibiotics (n = 55)	Deep Infection Rates: Systemic Antibiotics: 16% Systemic + Local: 4% No statistical significance was found neither between the two study groups overall nor within fracture classifications in these two groups	Addition of an antibiotic bead pouch reduced deep infection rates
Ostermann ²⁵	1995	Retrospective review of 1,085 open limb fractures over nine years. Study groups: Systemic Antibiotics (n = 240) Systemic and Local Antibiotics (n = 845)	Infection Rates: Systemic Antibiotics: 12% Systemic + Local: 3.7% (p < 0.001) Type III fractures displayed a significant decrease in infection rates: Systemic Antibiotics: 20.6% Systemic + Local: 6.5% (p < 0.001)	
Seligson ²⁶	1994	Retrospective review of 72 Type IIIc open fractures. Study groups: Systemic Antibiotics (n = 32) Systemic and Local Antibiotics (n = 40)	Wound Infection Rates: Systemic Antibiotics: 25% Systemic + Local: 5% (p < 0.05)	Administration of aminoglycoside-impregnated PMMA beads is of significant benefit in preventing infectious complications in severe injuries
Ostermann ²⁴	1993	Retrospective review of 704 open limb fractures over seven years. Study groups: Systemic Antibiotics (n = 157) Systemic and Local Antibiotics (n = 547)	Infection Rates: Systemic Antibiotics: 17% Systemic + Local: 4.2% (p < 0.001) Type III fractures displayed a significant decrease in acute wound infection rates: Systemic Antibiotics: 29% Systemic + Local: 6% (p < 0.001)	Antibiotic impregnated PMMA beads used prophylactically with systemic antibiotics prevented infectious complications in open fractures, especially in the use with Type IIIb fractures
Henry ²¹	1993	Retrospective review of 227 open limb fractures managed using an antibiotic bead pouch technique	Infection rates based on fracture classifications: Type I: 0% Type II: 3.6% Type III: 10.9%	The bead pouch technique decreases the incidence of infection. This technique is most useful in Type III fractures
Henry ²⁰	1990	Retrospective review of 404 open fractures over six years. Study groups: Systemic Antibiotics (n = 70) Systemic and Local Antibiotics (n = 334)	Infection Rates: Systemic Antibiotics: 21.4% Systemic + Local: 4.2% (p < 0.001) Type III fractures displayed a significant decrease in infection rates: Systemic Antibiotics: 43.9% Systemic + Local: 8.7% (p < 0.001)	

PMMA = polymethylmethacrylate

infection. One factor analyzed by Patzakis was time to debridement. Similar rates of infection were reported between early, defined as debridement within 12 hours, and delayed debridement, defined as debridement after 12 hours (6.8% and 7.1%, respectively). Although time to debridement was not an important predictor of infection rates in this study, early debridement was still recommended.

Bednar and Parikh⁴⁰ had similar findings in the association between time to primary management and subsequent infection rates. In a retrospective review of 82 open fractures of the lower extremity, the early debridement group (debridement within six hours) had an infection incidence of 9%, whereas the late debridement group (debridement after six hours) had an infection rate of 3.4%.

Table 4. Time to Debridement — Study Details

Author	Year	Study Design	Results	Conclusions
Enninghorst ⁶	2011	Retrospective, open tibia shaft fractures; n = 89 Debridement times: Early: <6 h Delayed: >6 h	No significant difference found in early vs delayed groups (no data shown) Time to operative treatment: Infected (n = 15): 7.87 h ± 4.7 Non-infected (n = 74): 7.95 h ± 4.5	Time to debridement was not a predictor of poor outcome
Pollak ⁴⁶	2010	Retrospective review of LEAP participants, n = 307 Debridement times: Early: <5 h Delayed: 5–10 h Late: 10–24 h	Incidence of infection, major infection: Early: 28%, 15.1% Delayed: 29%, 14% Late: 25.8%, 18.8%	Time to debridement did not affect incidence of infection. Infection related better to fracture grade
Sungaran ⁴⁵	2007	Retrospective review (n = 161) of open tibia fractures Debridement times: Early: <6 h Delayed: 6–12 h Late: 12–24 h	Total infection rate: 3.7% Incidence of infection: Early: 7.8% Delayed: 1.3% Late: 0% Of the infections that presented, 83% were from the early group	Infection rate was not associated with time to debridement
Charalambous ⁴⁴	2005	Retrospective review (n = 383) of open tibia fractures, mostly Type III fractures Debridement times: Early: <6 h Delayed: >6 h	No significant difference in incidence of infection was found between early and delayed groups Incidence of infection: Early: 28.8% Delayed: 25.6%	No difference was found in infection rates between early and delayed debridement patients
Spencer ²⁹	2004	Prospective audit of 115 open long bone fractures Debridement times: Early: <6h Delayed: >6h	Incidence of infection: Early: 10.1% Delayed: 10.8%	No difference found between delayed and early debridement in relation to infection
Khatod ⁴³	2003	Retrospective review of open tibia fractures (n = 106) Debridement times: Early: <6h Delayed: >6h	Infection rates (estimated): Early: 19% Delayed: 18% Average time to debridement (h): Infected vs not infected Type I: 9 vs 6.5 Type II: 5 vs 10 Type IIIa: 6.2 vs 10.4 Type IIIb: 4.7 vs 5.5 Type IIIc: 3.5 vs 3.8	Infection rates did not increase between early and delayed debridement groups
Harley ⁴²	2002	Retrospective review of open fractures using a multivariate and univariate regression analysis (n = 241) Debridement time: Early: <8 h Delayed: >8 h	Infection rates: Early: 9% Delayed: 10% Nonunion rates: Early: 21% Delayed: 16%	Time was not a significant factor in determining poor outcomes such as infection and nonunion
Kindsfater ⁴¹	1995	Retrospective review of Type II and III open tibia fractures (n = 47) Debridement time: Early: <5 h Delayed: >5 h	Infection rates: Early: 7% Delayed: 38% (p < 0.03)	A difference in infection rates between early and delayed debridement lends support to the standard 6 hour window
Bednar ⁴⁰	1993	Retrospective review of open long bone fractures (n = 82) Debridement time: Early: <6 h Delayed: >6 h	Infection rates: Early: 9% Delayed: 3.4%	Early debridement does not hold a benefit over delayed debridement in relation to incidence of infection
Patzakis ⁴	1989	Retrospective review of open fractures (n = 1104) Debridement time: Early: <8 h Delayed: >8 h	Infection rates: Early: 6.8% Delayed: 7.1%	Time to debridement is not an important factor in determining risk of infection, however authors support early debridement

LEAP = lower extremity assessment project

In 1995, however, Kindsfater and Jonassen⁴¹ were able to support the standard “six hour” rule for operative treatment in a retrospective review that analyzed the development of osteomyelitis in Type II and III open fractures following either early (<5 hours) or delayed (>5 hours) debridement. In Type II open fractures, 10% of the early group and 33% of the delayed group developed osteomyelitis. In Type III open fractures, no one in the early group developed osteomyelitis, whereas osteomyelitis developed in 41% of the delayed group.

Almost a decade later, Harley et al.⁴² conducted a retrospective review comparing open fractures treated within eight hours and those treated after eight hours. Time to debridement had no relationship to open fracture complications such as deep infection and fracture nonunion. Deep infection rates reported from a univariate analysis were 9% in the early group compared to 10% in the late group. Non-union analyses were also similar between early and late debridement, reported at 21% and 16%, respectively.

Khatod and colleagues⁴³ studied 106 open fractures to determine the relationship between time to operative treatment and infection and found no difference in infection rates between open fractures subjected to debridement within six hours compared to those after six hours.

A five-year prospective audit of 115 open fractures was conducted by Spencer et al.²⁹ which supported previous studies. Infection rates in early and late debridement groups were comparable. There was a 10.1% infection rate in fractures debrided within six hours, whereas there was a 10.8% infection rate in those debrided after six hours.

In reviewing 383 open tibial fractures, Charalambous et al.⁴⁴ found no significant difference in the incidence of infection between patients debrided within six hours and those debrided after six hours (28.8% vs 25.6%, respectively).

Similarly, Sungaran and colleagues⁴⁵ found no association between time to debridement and infection rates in a retrospective review of 161 patients with open tibia fractures sorted into three groups: debridement from 0–6 hours, 6–12 hours and 12–24 hours. A total infection rate of 3.7% was reported, most of which occurred in the 0–6 hour debridement group.

In 2010, a sub-study of the lower extremity assessment project (LEAP) reviewed 315 Type III open fractures of the lower extremity to evaluate the relationship between time to operative treatment and infection rates. Pollak et al.⁴⁶ found that time to debridement did not influence infection rates. There was a 15.1% incidence of major infection, such as osteomyelitis, in groups debrided within five hours; 14% incidence of infection in the group with a 5–10 hour delay to debridement; and 18.8% incidence in groups debrided between 10–24 hours. Similar to previous studies, Pollak et al. did not find an association between infection and the timing of debridement following injury.

In the most recent study, Enninghorst and colleagues⁶ explored predictors of poor outcomes in open tibia fractures

using a retrospective study of 89 patients. Both univariate and multivariate analyses failed to detect a statistically significant difference in infection rates with early and late debridement times. Similar to previous studies, although no relationship was found between time to debridement and infection rates, the author recommends early debridement when possible.

Irrigation — Solutions and Delivery

The database search resulted in a total of two studies that met the criteria for irrigation techniques in the management of open fractures in adults (Table 5).

Anglen⁴⁷ conducted a prospective randomized clinical control study assessing the effectiveness of different irrigation solutions, specifically focusing on antimicrobial additives compared to a non-sterile soap. A total of 458 open fractures of the lower extremity were used in the study. No significant differences were found between groups receiving an antimicrobial additive compared to those receiving a detergent in infection rates (18% vs 13%) and bone healing (25% vs 23%). Although, patients that received irrigation with the antimicrobial solution had a wound healing problem incidence of 9.5%, whereas those that received a detergent for irrigation had a 4% incidence. Therefore, Anglen concludes that there is no advantage to the use of antibiotic irrigation solutions as there is an increased risk of wound healing complications.

In 2011, a multicenter pilot study comparing alternative irrigation solutions and pressures was tested. As part of the fluid lavage in patients with open fracture wounds (FLOW) study, investigators⁴⁸ conducted a blinded randomized 2 x 2 factorial pilot in which 111 patients were treated with either detergent or normal saline and either high- or low-pressure lavage. Rates of primary outcome, including infection, wound healing problems or nonunion, were similar between groups that received a detergent versus those that received saline as the irrigation solution (23% vs 24%). When comparing pressure settings for irrigation, 28% in the high-pressure irrigation group had a primary outcome, whereas 19% of low-pressure group had an outcome.

Discussion

Prophylactic Antibiotic Duration

Despite an association between prolonged antibiotic use and poor outcomes such as the development of antibiotic resistant infections and host toxicity,^{9,17} there have been a limited number of studies that examine the relationship between prophylactic antibiotic duration in the early management of open fractures and subsequent complications. In the two studies found by the search described above, only one was a randomized control study comparing the efficacy of a short duration and long duration prophylactic antibiotic therapy; the other retrospectively analyzed the duration of prophylactic antibiotics in 1,492 open fractures. Both of

Table 5. Irrigation Techniques — Study Details

Author	Year	Study Design	Results	Conclusions
Bhandari ⁴⁸	2011	A randomized multicenter pilot developed by FLOW comparing irrigation solutions and techniques; n = 111 Patients divided into four groups: SL = saline, low-pressure SH = saline, high-pressure CL = castile, low-pressure CH = castile, high-pressure	Primary outcome (infection, wound healing, nonunion) rates: S: 24% C: 23% H: 28% L: 19%	The castile soap group had a 23% hazard risk reduction compared to saline. Favor use of castile soap and low-pressure (6–10 psi) lavage.
Anglen ⁴⁷	2005	Prospective randomized study comparing the detergent and antibiotic solutions for irrigation of open wounds; n = 458 Groups: B: bacitracin (antibiotic) C: nonsterile castile soup (detergent)	Infection rates: B: 18% C: 13% Bone Healing Delays: B: 25% C: 23% Wound Healing Problem Rates: B: 9.5% C: 4%	No difference was found between infection rates and bone healing after either antimicrobial or detergent irrigation solutions. However, the antibiotic group had an increased risk of wound healing problems. Therefore, an antimicrobial irrigation solution has no advantage over a detergent and may result in complications.

FLOW = fluid lavage in patients with open fracture wounds; psi = pounds per square inch

these studies concluded that a shorter duration of prophylaxis is just as effective in preventing infection as longer duration therapies.^{38, 39} However, each study had limitations. Many uncontrollable factors were present in both studies as the preferences and techniques of the surgeon, often determined by the standard practice at the trauma center, influenced the surgical treatment. Additionally, neither study assessed the risks of prolonged prophylactic antibiotic therapy. Dellinger et al.³⁸ briefly mention risks, such as increased antibiotic-resistant infections and increased costs, occurring in about 5–17% of patients, in their discussion and use this as support of shorter duration therapies, but neglect to measure these outcomes in their study population. Dunkel and colleagues³⁹ excluded infections that occurred after two months or were considered nosocomial from their study, even though other clinical studies look beyond four months to assess wound infection and osteomyelitis. Furthermore, *S. aureus*, the leading pathogenic cause of nosocomial infections,^{17, 49} has been found to be the predominant microbe isolated from open fracture wounds.^{3, 4, 43, 50} Restriction to infections within two months and exclusion of nosocomial infections may overlook the effects of antibiotic resistant microbes, which can put a patient at greater risk for infection.⁵⁰

In 1998, the Eastern Association for the Surgery of Trauma (EAST) proposed guidelines,¹⁴ updated recently in 2011,¹³ for prophylactic antibiotic use in the management of open fractures that describe recommended classes and durations of antibiotics based on fracture grade (Table 1, Appendix 1a). The Surgical Infection Society (SIS) released similar recommendations in 2006 using a systematic review of the literature from 1985–1997 (Appendix 1b).⁹ According to recent reports, however, these guidelines are not always followed in practice. Barton et al.¹⁹ performed a retrospective review of patients from 2004–2008 assessing the adherence to the guidelines set forth in 1998 by the EAST workgroup.

The study reported that 28.5% of patients received compliant therapy. Noncompliance to the guidelines was typically due to prolonged duration of the correct coverage antibiotic, thus exceeding the recommendations. This was associated with increased hospital and intensive care unit length of stay and the number of surgeries performed. Unfortunately, the duration of antibiotics was not measured after it was determined to be noncompliant to the recommendations, and therefore, the length of antibiotic therapy could not be related to the complications reported. Lavelle et al.⁵¹ similarly showed inconsistency with prophylactic antibiotic use in practice, with greater variability in more severe fracture classifications, following a survey of orthopaedic residency programs. This study, however, did not assess outcomes as a result of this variation.

Environmental factors can also influence wound healing, development of postoperative infections and union of the fracture. Diabetes, smoking, obesity, immunosuppression and malnutrition, commonly seen in the patient population at TUH, are several risk factors for infectious complications and poor wound healing.^{17, 52–56} The appropriate duration of prophylactic antibiotic administration, however, has yet to be elucidated in these population groups. Surgeons have reported making exceptions to current recommendations when they judged that an extended antibiotic regimen was needed for these patients.¹⁹ As previously mentioned, prolonged antibiotic use does not decrease the risk of surgical site infections and has been associated with complications such as antibiotic resistant infection, toxicity and allergic reactions, which may put this population at a greater risk for poor outcomes following open fracture management. More clinical research is needed to determine the recommended prophylactic antibiotic therapy for populations at an increased risk for infection and impaired wound healing.

After review of the studies supporting a shorter duration of prophylactic antibiotic use and comparing current stan-

dards of practice with the recommendations proposed by EAST and SIS workgroups, guidelines were created for prophylactic antibiotic administration in the management of open fractures that modeled those proposed the EAST workgroup.

Local Antibiotic Delivery

Local antibiotic therapy is an effective method for delivering a high concentration of antibiotic to the wound site while maintaining low systemic levels.^{16, 21, 22, 27} Impaired vascularity and devitalized bone, common characteristics of severe open fractures, can result in increased growth of organisms¹¹ and poor delivery of intravenous antibiotics.²³ The use of local antibiotics as an adjunct to prophylactic systemic antibiotics in severe open fractures nonetheless remains a debate, despite the advantages such therapy may provide. Benefits of adjunct local antibiotic delivery in reducing the incidence of infections are supported by several retrospective studies^{20–22, 24–26} and a pilot prospective study;²³ however, limitations of these studies prevent the standardization of local antibiotic delivery in the management of open fractures.⁹ A difference in soft tissue wound management between study groups has been noted as a great limitation of these studies.^{20, 21, 23–26} For effectively high concentrations of antibiotic, antibiotic beads should be placed in a closed wound environment,²⁷ often packed into the dead space of the wound and sealed with a porous plastic film,^{21, 22} although other techniques have been described. Variations in wound closure techniques between the study groups may influence infection rate outcomes; however, more recent studies have demonstrated that wound closure remains an independent predictor of infection.^{57, 58} Another weakness of the studies includes nonrandomization of antibiotic treatment, as the implantation of antibiotic-impregnated beads was determined by the surgeon and bead availability,^{20, 21, 24–26} creating a selection bias. Nonetheless, these studies support the supplemental use of local prophylactic antibiotic administration in severe open fracture management.

Despite the limited number of clinical studies evaluating the benefits of co-administration of local antibiotics with prophylactic systemic antibiotics in the management of open fractures, antibiotic-loaded beads appear promising through a decreased risk of the complications associated with prolonged antibiotic therapy. These beads can achieve high local levels while maintaining low systemic levels of antibiotics.^{16, 21, 22, 27} Therefore, concerns of systemic toxicity, allergic reactions to antibiotics and the development of antibiotic-resistant nosocomial infections, which have been reported to occur rarely with this local administration technique,^{17, 22, 27} can be minimized. Use of local antibiotics when an extended duration of antibiotics would otherwise be indicated,⁹ such as in cases of severe open fractures or in patients with factors affecting wound healing, may thus prove beneficial.

Time to Debridement

Recent clinical studies sought to reevaluate the evidence behind the standard “six-hour” window between the time of injury and time of initial debridement. This urgency has been based on bacterial culture and reproductive data in animal wound models, which describe a relationship between the levels of bacterial contamination, time and infection.^{59–61} At six hours, bacterial levels that reach greater than 10⁵ organisms per gram of tissue can result in infection whereas lower levels are below the infection-causing threshold.⁶⁰ Clinical studies, however, have not been able to provide evidence for the standard six-hour window of time to debridement.

All but one of the papers reviewed failed to find an association between infection and time to debridement as animal studies previously described.^{4, 6, 29, 40, 42, 44, 46} Although studies varied slightly in outcome measures of infection and the times considered as early versus delayed debridement, infection rates between early and delayed debridement study group were not significantly different. Furthermore, several studies reviewed only open fractures of the lower limb,^{6, 40, 43–46} whereas others included open fractures of both lower and upper extremities.^{4, 29, 42} Despite these differences, infection rates reported were similar to those previously reported.^{2, 3} An additional limitation of these papers includes variation in surgical techniques and treatment used between study groups, resulting in uncontrollable confounding factors.

Unlike other clinical studies, Kindsfater and Jonassen⁴¹ found a significant difference in infection rates between early (≤ 5 hours) and late (> 5 hours) debridement groups, lending support to earlier animal studies that describe an association between time to debridement and the development of infection. However, this study only reviewed open tibia fractures of Gustilo-Anderson classification II and III and used a more limited definition of infection, measuring only the incidence of osteomyelitis development. Therefore, this study cannot be generalized to all open fractures.

However, in further support of early debridement, a recent study using an open femur fracture model in rats was conducted by Penn-Barwell et al.⁶² which sought to control for confounding factors such as surgical techniques, as criticized in clinical studies. A significant increase in positive cultures was found in animal groups that received surgical debridement between 2–6 hours compared to those that received surgical debridement within two hours. This experimental model was not without its limitations, however. The open fracture and associated wound were created surgically, minimizing the extent of soft tissue damage and thus preventing its applicability to more severe open fractures. Furthermore, infections rates reported ranged from 50–100% which is very high compared to those reported in clinical studies.^{2–4} Additionally, sample sizes were small, with a total of 10 animals per experimental group. Though this experimental design attempted to demonstrate the significance of

urgent debridement on the prevention of infection, it failed to mimic other elements of an open fracture seen clinically.

Despite a lack of clinical evidence for the six-hour rule, many clinical studies continue to suggest early debridement when possible. In 2009, Ricci and colleagues²⁸ demonstrated an association between after-hours surgeries and a higher incidence of complications. Thus, to prevent complications following the management of open fractures, early debridement and operative treatment are recommended for all open fracture classifications when adequate resources are available.

Irrigation: Solutions and Delivery

Copious irrigation is one of the most important steps in the management of open fractures;^{16, 30, 31, 36} however, there is great variation in the techniques used. In an international survey of orthopaedic surgeons in 2008, no standard practice was found amongst surgeons with respect to irrigation techniques. Differences were found in irrigation volume, solution and delivery for each open fracture classification.³²

A limited number of clinical studies assess the efficacy of the various irrigation techniques. The search described above yielded two clinical studies that met the inclusion criteria, which included a randomized control study comparing irrigation solutions⁴⁷ and a randomized pilot study comparing irrigation delivery and solutions.⁴⁸

The delivery of irrigation solution remains a debate. The 2008 FLOW survey reports that a majority of surgeons use low-pressure lavage, although definitions of “low” remain unclear.^{32, 33} When comparing pressure settings for irrigation, the FLOW pilot study demonstrated a greater incidence of infection, wound healing or nonunion in the high-pressure (25–30 pounds per square inch (psi)) irrigation group when compared to the low-pressure (6–10 psi) group.⁴⁸

High- and low-pressure lavage were also compared in *in vitro* studies using human and canine tibia sections. High-pressure lavage resulted in more fissures and defects in the bone than low-pressure lavage; however, when compared to controls that did not receive pressure lavage, low-pressure lavage also showed increases. The number and size of defects were proportional to the pressure; however, it is unclear whether this relationship is direct. This study also illustrated that both high- and low-pressure lavage were equally effective at removing bacteria for up to three hours. After six hours, however, low-pressure lavage decreased in effectiveness, and a higher pressure was recommended.³³ In 2002, Adili and colleagues³⁵ analyzed the biochemical effects of high-pressure irrigation on fracture healing *in vivo* and found decreased mechanical strength of bone when compared to bulb syringe irrigation. Therefore, although high-pressure lavage is effective at removing bacteria, it can be harmful and thus low-pressure lavage (6–10 psi) is recommended for the irrigation of open fracture wounds.

Current irrigation solutions include saline, antimicrobial and antiseptic additives and detergent. In a comparison of castile soap, a detergent, and an antimicrobial irrigation solution in a clinical prospective randomized study of open fractures, the detergent proved to be as efficacious in preventing infection, and did not result in wound healing delays as the antimicrobial agent did.⁴⁷ Similarly, the FLOW pilot study demonstrated a decreased relative risk in the development of infection with the use of castile soap compared to saline.⁴⁸

Several animal studies also support the use of detergent over antibiotic, antiseptic and saline irrigation solutions.^{33, 36, 63} Bhandari and colleagues assessed the effect of different irrigation solutions on bone structure and their effectiveness in removing bacteria using an *in vitro* model. The use of detergent with low-pressure lavage proved more effective at removing adherent bacteria up to six hours over saline. Additionally, the detergent solution had less of an impact on bone healing, measured by the number and function of osteoblasts and osteoclasts.³⁴ Similarly, Burd et al. showed that detergents decrease the bacterial load and number of infections in an animal wound model when compared to saline.⁶³

Despite evidence of the superiority of detergent over saline and the potential for harm associated with antimicrobial and antiseptic agents, the FLOW survey reports that saline remains the solution preference of most surgeons, followed by antimicrobial agents and then antiseptic; detergents remain the least commonly used.³² The limited use of detergents in practice is likely due to its difficulty in accessibility. Therefore, in circumstances where detergent is unavailable, saline can be used as an alternative. More importantly, antibiotic and antiseptic additives should not be used in irrigation solutions due to their potential risks.

The volume of irrigation solution has been least studied clinically. In 2001, Anglen reported volumes used for each Gustilo fracture classification based on convenience of a three liter (L) irrigation bag size: Type I 3L; Type II 6L and Type III 9L.³⁰ The FLOW survey reported that 63.9% of surgeons preferred to use 3L or less for Type I fractures, 50.1% used 3–6L for Type II fractures and 41.3% preferred to use 3–6L also for Type III fractures.³² Clinical study methods illustrate a range from 3–9L when irrigation volumes were reported,^{29, 39–43, 47} one of which used a minimum of 9L saline per wound.³⁹ Animal studies have demonstrated that increased volumes of irrigation solution aid in the removal of bacteria and dirt,³⁰ and thus more effectively decrease the bacterial load in the wound. However, no clinical data can provide evidence to support these ranges.

Thus low-pressure lavage (6–10 psi) using either saline or detergent (i.e., castile soap) with increased volumes for more severe injuries proves to be the favored irrigation technique for effectively removing bacteria from a contaminated wound, and thus preventing infection and other complications.

Summary

Recommendations provided (Table 6) are based on a review of the above clinical and animal studies, with the data from clinical study considered with more weight over animal models.

Prophylactic antibiotics should be administered as soon as possible after injury, preferably within three hours. The drug class and duration of antibiotic given is determined by the severity of the open fracture, as described by Gustilo and Anderson. Antibiotic recommendations have been adapted from the updated EAST guidelines after review of the information provided and consideration of current practice standards. Type I and Type II fractures should be given gram-positive coverage, such as a first generation cephalosporin, for no more than 24 hours after wound closure. Gram-negative coverage, such as an aminoglycoside, should be added for Type II fractures. Type III fractures should be administered both gram-positive and gram-negative coverage, such as a cephalosporin and an aminoglycoside, which should be continued for 72 hours after injury and no more than 24 hours after wound closure. Fluroquinolones should not be used, as they offer no advantage over cephalosporins and aminoglycosides and may have a negative impact open fracture outcome. Local antibiotic delivery may prove beneficial in Type III open fractures and in patient populations where prolonged antibiotic therapy is otherwise indicated. Emergent surgical intervention should occur if resources and an experienced surgical team are available. A low-pressure (6–10 psi) pulsatile lavage system with either saline or detergent (i.e., castile soap) using increased volumes of solution for more severe fractures should be used to irrigate the wound prior to fixation. If irrigation occurs after six hours, a

higher pressure may be necessary to adequately reduce the bacterial load.

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Table 6. Summary Guidelines and Recommendations

Fracture Classification	Type I	Type II	Type IIIa-c
Prophylaxis Antibiotic	First generation cephalosporin (gram-positive coverage), continued for 24 hours after wound closure.	First generation cephalosporin (gram-positive coverage), continued for 24 hours after wound closure. The addition of a once-daily aminoglycoside (gram negative coverage) is safe and effective.	First generation cephalosporin (gram-positive coverage) and aminoglycoside (gram-negative coverage) continued for 72 hours after injury, but no more than 24 hours after soft tissue coverage of the wound. Penicillin is recommended for farm related injuries, with soil or fecal matter contamination.
	Fluroquinolones should not be used as they offer no advantage over cephalosporins and aminoglycosides and may have a negative impact open fracture outcome.		
	Local antibiotic delivery may prove beneficial in Type III open fractures and in patient populations where prolonged antibiotic therapy is otherwise indicated.		
Time to Debridement	Debridement should occur in an emergent fashion if the resources and a prepared surgical team are available. Early debridement, before six hours, is recommended but not supported by current evidence.		
Irrigation Volume	<3L	3–6L	>6L
Irrigation Solution	Low-pressure (6–10 pounds per square inch) lavage with saline or detergent (i.e., castile soap) is recommended if debridement occurs within six hours after injury. After six hours, a higher pressure system may be necessary to adequately reduce the bacterial load. Antibiotic and antiseptic additives should not be used due to potential risks.		

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Appendix

1a. Eastern Association for the Surgery of Trauma (EAST) Guidelines

Luchette et al., 2000¹⁴:

Type I: Pre-operative dosing with prophylactic antibiotics as soon as possible after injury for coverage of gram-positive organisms (Level 1). Antibiotics should be discontinued 24 hours after wound closure (Level 2).

Type II: Pre-operative dosing with prophylactic antibiotics as soon as possible after injury for coverage of gram-positive organisms (Level 1). Antibiotics should be discontinued 24 hours after wound closure (Level 2).

Type III: Pre-operative dosing with prophylactic antibiotics as soon as possible after injury for coverage of gram-positive organisms (Level 1). Additional coverage for gram-negative organisms should be given. High dose penicillin should be added to the antibiotic regimen when there is a concern for fecal/clostridial contamination, such as in farm related injuries (Level 1). Antibiotics should be continued for only 72 hours after the time of injury or not more than 24 hours after soft tissue coverage of the wound is achieved, whichever occurs first (Level 2).

Update — Hoff et al., 2011¹³:

Type I: Systemic antibiotic with gram-positive coverage initiated as soon as possible after injury (Level 1).

Type II: Systemic antibiotic with gram-positive coverage initiated as soon as possible after injury (Level 1). Once-daily aminoglycoside dosing is safe and effective (Level 2).

Type III: Systemic antibiotic with gram-positive coverage initiated as soon as possible after injury. Gram-negative coverage should be added. High-dose penicillin added in the presence of fecal/clostridial contamination (Level 1). Antibiotics should be continued for 72 hours after injury or not >24 hours after soft tissue coverage has been achieved (Level 2). Once-daily aminoglycoside dosing is safe and effective (Level 2).

In addition, fluoroquinolones offer no advantage over cephalosporin and aminoglycoside agents but may have detrimental effects on fracture healing and result in high infection rates in Type III open fractures (Level 1).

1b. SIS (Surgical Infection Society) Recommendations

Hauser et al., 2006⁹:

Type I: Administration of a first generation cephalosporin (or similar gram-positive coverage) for 24–48 hours perioperatively is a safe and effective prophylactic choice (Level 1).

Type II: Administration of a first generation cephalosporin (or similar gram-positive coverage) for 48 hours perioperatively is a safe and effective prophylactic choice (Level 2). A single broad-spectrum agent given pre-operatively and extended for 48 hours post-operatively is a safe and effective prophylactic choice (Level 3).

Type III: Administration of a first generation cephalosporin (or similar gram-positive coverage) for 48 hours perioperatively is a safe and effective prophylactic choice (Level 2). A single broad-spectrum agent given pre-operatively and extended for 48 hours post-operatively is a safe and effective prophylactic choice (Level 3).

Insufficient data to support the use of gram-negative antibiotics against bacilli as prophylaxis in open fractures, prolongation of prophylactic antibiotic use past the initial perioperative period, administration of prophylactic penicillin in *Clostridium*-prone injuries, use of antibiotic beads in the management of open fractures, and antibiotic therapy based on wound cultures.

2. Recommendation Levels of Evidence (from the EAST and SIS Guidelines)

Level 1:

EAST Recommendations: based on Class I data (prospective, randomized, controlled study) or a preponderance of Class II data (prospective, randomized, non-blinded trials); based on the available scientific evidence alone

SIS Recommendations: based on sufficient Class I and Class II data (any prospective or randomized-trial data)

Level 2:

EAST Recommendations: supported by Class II data or a preponderance of Class III evidence (retrospectively collected data, database and registry reviews, and meta-analysis); justified by the available scientific evidence and strongly supported by expert critical care opinion

SIS Recommendations: based on sufficient Class I and Class II data

Level 3:

EAST Recommendations: supported by Class III data; supported by available data, but inadequate scientific data are available

SIS Recommendations: based on sufficient Class I, Class II, and Class III data (Class III data are purely observational or retrospective studies)

Medical Student Research Project

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Initial Management of Femoral Shaft Fractures in the Multiply Injured Patient: Clinical Practice Guidelines

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Abstract

Background: The optimal management of femoral shaft fractures in multiply injured patients remains controversial. The purpose of this research is to create a clinical guideline for the initial treatment of femoral shaft fractures at Temple University Hospital that helps identify the “borderline” patient and outlines the best management for borderline patients, patients with concomitant chest injuries, and patients with concomitant head injuries.

Methods: A systematic review of published English-language studies using MEDLINE (1946–2013) was done using medical subject headings: *femoral fractures*, *multiple traumas*, *respiratory distress syndrome*, *adult fracture fixation*, *traction*, *external fixator*, *thoracic injuries*, and *craniocerebral trauma*. Studies pertaining to the borderline patient, provisional stabilization of femoral shaft fractures, or the timing and/or method of definitive fixation of femoral shaft fractures in multiply injured patients were selected for review.

Results: Twenty reviews met inclusion criteria and were grouped into borderline patient (six studies), provisional stabilization (five studies), timing of definitive fixation in borderline (three studies), concomitant chest-injured (eight studies), and concomitant head-injured patients (seven studies), and physiological indicator of patient stability (one study) with some overlap.

Conclusion: Borderline patient characteristics were added to previously published descriptions. External fixation (EF) and skeletal traction (ST) were identified as provisional stabilization methods for borderline and severely injured patients that are not resuscitated quickly. Reported time to conversion from provisional stabilization to definitive intramedullary nailing (IMN) in borderline patients were less than one week. The optimal timing for IMN in both chest and head-injured patients with femoral shaft fractures remains controversial. However, as long as the patient is adequately resuscitated before surgery, the evidence showed early IMN within 24 hours of injury was associated with fewer complications than delayed procedures in patients with either concomitant

chest or head injuries. Multiply injured patients with pre-operative lactate level <2.5 mmol/L demonstrated fewer complications after an IMN procedure than those with lactate level >2.5 mmol/L. The collective evidence was used to create practice guidelines to be implemented at Temple University Hospital.

Introduction

Femoral shaft fractures are serious injuries usually caused by high-energy trauma, and early medical attention helps prevent subsequent morbidity or mortality. The standard of treatment for this type of fracture is definitive fixation with an intramedullary nail (IMN).¹ However, differences in clinical outcomes between subgroups of patients with femoral shaft fractures have been observed. Historically, it was shown that patients with femoral shaft fractures and concurrent head trauma were at increased risk of mortality compared to patients with isolated femoral shaft fractures.² A recent study has shown that femoral fractures and associated injuries continue to predict increased risk of morbidity and mortality.³ Today, there is debate over the best initial management and optimal timing of definitive fixation in multiply injured patients who have femoral shaft fractures associated with other traumatic injuries.

For the past few decades, discussion regarding the management of these multiply injured patients has mainly focused on the timing of definitive fixation of the fracture. Bone et al.⁴ conducted a prospective study in the late 1980s which showed multiply injured patients with femoral shaft fractures treated with IMN within 24 hours after injury trended to a lower incidence of Adult Respiratory Distress Syndrome (ARDS) and pulmonary dysfunction compared to delayed IMN. This finding contributed to a movement toward early IMN procedures for all femoral shaft fractures, even in the multiply injured patient, called “Early Total Care” (ETC). This approach was questioned by Pape⁵ in the early 1990s after he observed that multiply injured patients with a femoral shaft fracture and associated chest injury had an increased incidence of ARDS after early reamed IMN compared to delayed treatment. In the study, “borderline patients” were introduced as the subpopulation of femoral

shaft fracture patients with associated injuries that predispose them to developing major complications.

It was thought that early reamed IMN produced a “second hit” of trauma too soon after the initial trauma, which could then overwhelm the patient and lead to complications such as ARDS.^{6,7} Another treatment methodology called “Damage Control Orthopedics” (DCO) was coined by Scalea⁸ to describe the method of using external fixation (EF) as a means of temporarily stabilizing a femoral fracture before converting to definitive IMN. This approach was thought to protect the borderline patient by reducing the initial operative burden and lowering the systemic inflammatory response compared to an IMN procedure.⁹

As orthopaedics treatment of this injury pattern has evolved, subgroups of patient populations have demonstrated that one treatment paradigm or method does not fit all in the case of multiply injured patients with femoral fractures. The injury patterns that receive attention in the literature are borderline patients and patients with concomitant chest and/or head injuries. These multiply injured femoral shaft fracture patients are a diverse population, and optimal treatment of the femoral shaft fractures may require an individualized approach. The purpose of this research was to create a clinical guideline that can help identify the “borderline” patient and outline the best provisional treatment methods for borderline patients, patients with concomitant chest injuries, and patients with concomitant head injuries.

Methods

Literature searches were conducted using MEDLINE (1946 to July 12, 2013) and the Cochrane Library databases (July 12, 2013). The following medical subject headings and search strategies were used: *femoral fractures* [MeSH:NoExp] AND *multiple traumas* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *multiple traumas* [MeSH] AND *respiratory distress syndrome, adult* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *multiple traumas* [MeSH] AND *fracture fixation* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *multiple traumas* [MeSH] AND *traction* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *multiple traumas* [MeSH] AND *external fixator* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *fracture fixation* [MeSH] AND *thoracic injuries* [MeSH]; *femoral fractures* [MeSH:NoExp] AND *fracture fixation* [MeSH] AND *craniocerebral trauma* [MeSH].

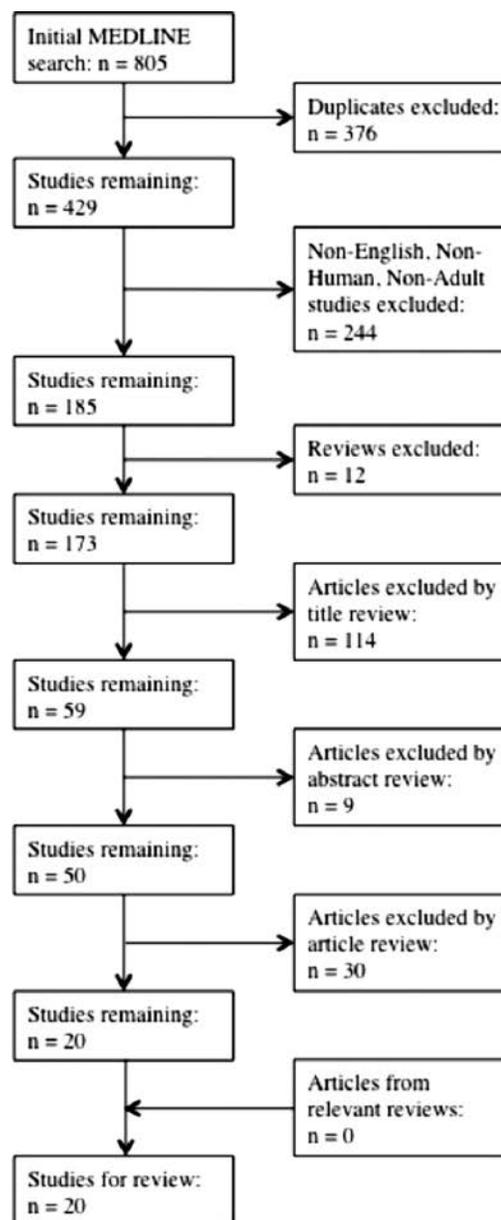
Searches were restricted to articles that were written in English and analyzed adult human patients. Reviews were excluded from analysis. Searches were not restricted by geography or date. Title, abstract, and article reviews were done in succession to select relevant articles that pertained to the borderline patient, provisional stabilization of femoral shaft fractures, or the timing and/or method of definitive fixation of femoral shaft fractures in multiply injured patients. Additionally, bibliographies of relevant review articles were surveyed to find studies not found through the computerized search.

Results

Search Results

Twenty articles met selection criteria (Figure 1) for this review and were then divided into the following topics: identifying the borderline patient, provisional management of femoral shaft fracture, and timing of definitive fixation. When appropriate, studies were used in multiple topics. Unless otherwise noted, studies described below were retrospective analyses of patients selected from single or multi-center trauma databases.

Figure 1. Literature Search Process and Results



The Borderline Patient

Borderline patient characteristics were selected from patients that were associated with a greater risk of complications after early IMN or were non-randomly treated with DCO. Patients with increased risk of complications after early IMN had an associated thoracic injury (Abbreviated injury scale (AIS) thorax ≥ 2)⁵ or a severe abdominal injury (AIS ≥ 3).^{10, 11} A prospective observational study of trauma patients with femoral shaft fractures found multiple IM nailing procedures and associated thoracic injury as independent risk factors for respiratory failure.¹² Patients treated with EF at a trauma center in Baltimore, MD had lower mean admission Glasgow Coma Score (GCS) (11), higher Injury Severity Scale (ISS) (26.8) scores, were more likely to have been in shock, had an AIS Head ≥ 3 ,⁸ and presented with higher lactate levels at admission¹³ than their early definitive IMN treated counterparts. These characteristics are presented along with previously published descriptions from a review by Pape¹⁴ (Table 1).

Table 1. Patient Description to Identify the “Borderline” Patient (modified from Pape et al.)¹⁴

Polytrauma + ISS >20 and additional thoracic trauma (AIS >2)
Polytrauma with abdominal/pelvic trauma (> Moore 3, AIS $\geq 3^*$) and hemodynamic shock (initial BP <90 mmHg)
ISS 40 or above in the absence of additional thoracic injury
Radiographic finding of bilateral lung contusion
Initial mean pulmonary arterial pressure >24 mmHg
High presenting lactate level*
Multiple IMN procedures at one time*

*Author added

ISS = Injury Severity Scale score; AIS = abbreviated injury scale; BP = blood pressure; IMN = Intramedullary Nailing

Provisional Stabilization of Femoral Shaft Fractures

Two methods of provisional stabilization before conversion to IMN were described in the reviewed studies: EF and skeletal traction (ST) (Table 2). Studies that compared EF (as part of a DCO protocol) with early IMN found worse⁸ or comparable^{15, 16} outcomes after EF. However, subgroup analysis in one of these studies revealed lower incidence of acute lung injury (ALI) after EF in borderline patients.¹⁵ The EF (or DCO) group was significantly more seriously injured upon admission in each of these studies. Comparison of provisional ST and early IMN showed that ST patients were more seriously injured than their IMN treated counterparts.¹⁷ In this study, patient outcomes were worse in the ST group than early IMN group, but comparable with the Damage Control-External Fixation (DC-EF) group.

Patients with femoral shaft fractures and concomitant chest injuries (thoracic AIS >2) treated with DCO had significantly higher rates of death and longer Intensive Care Unit (ICU) length of stay (LOS) compared to those treated with IMN, but the DCO group was significantly more severely injured upon admission.¹³

The literature search did not yield any studies that addressed provisional stabilization of femoral fractures in patients with concomitant femoral shaft fractures and head injuries.

Timing to Definitive Stabilization of Femoral Shaft Fractures — Borderline Patient

Three studies that reported times to conversion from provisional stabilization to definitive IMN in borderline patients were reviewed (Table 3). One study reported conversion from EF to IMN in a median of four days⁸ with normalized lactate (value not stated) and mean cardiac index 5.9 L/min per m², while another study reported conversion from EF in a mean of 5.04 days¹⁷ and from ST in a mean of 4.08 days (no physiologic criteria were stated). One study compared infection rates in DCO patients and found significantly more pin-site contaminations without clinical consequence on patients converted to definitive IM nailing after 14 days compared to before 14 days.¹⁸ Patients were converted from external fixation at the senior surgeon’s discretion based on hemodynamic stability, local soft-tissue status, presence of systemic complications, and logistic availability of staff and operating rooms.

Timing to Definitive Stabilization of Femoral Shaft Fractures — Concomitant Chest Injury (Non-borderline)

Eight studies analyzed the timing of IMN in chest-injured patients by comparing presence or absence of femoral shaft fracture and treatment, early vs. delayed treatment, or early IMN vs. DCO (Table 4). Three studies showed that chest-injured patients with femoral shaft fractures treated with early IMN did not suffer worse outcomes compared to chest-injured patients without femoral shaft fractures.¹⁹⁻²¹ Two studies found either an increased risk of ARDS⁷ or a trend to higher mortality²² after early IMN (<24 hours of injury) compared to delayed IMN. In contrast, two other studies found no difference in mortality rates between early and delayed IMN treated patients²³ as well as lower rates of pulmonary complications after early IMN compared to delayed treatment.^{11, 23} O’Toole et al.¹³ found that early IMN (mean 14.0 hours from admission) treated chest-injured patients had better outcomes compared to DCO treated patients. Three of these studies described physiologic criteria that were met before definitive IMN including normalized lactate levels (<2.5 mmol/L), hemodynamic stability, and respiratory stability.^{11, 13, 21}

Timing to Definitive Stabilization of Femoral Shaft Fractures — Concomitant Head Injury

Seven studies analyzed the timing of IMN in chest-injured patients by comparing early vs. delayed treatment or presence or absence of femoral shaft fracture and treatment (Table 5). Two studies were unable to find any adverse effects on mortality or ICU LOS between head-injured patients with or without femoral shaft fractures treated by

Table 2. Provisional Stabilization of Femoral Shaft Fractures

Author, Year	Comparison	Relevant Results	Conclusions & Notes
Borderline Patient			
Scalea et al., 2000 ⁸	<ul style="list-style-type: none"> External Fixation (EF) n = 43 Intramedullary nailing (IMN) n = 281 	<p>EF vs. IMN:</p> <ul style="list-style-type: none"> EF group significantly more severely injured (higher ISS, lower GCS, higher % in shock, higher AIS-Head score) ($p < 0.01$) EF group had significantly higher rate of ICU stay, longer hospital LOS ($p = 0.001$), and trend to more deaths (not 2° to fracture management) 	<ul style="list-style-type: none"> External fixation is reserved for more seriously injured patients (Damage Control Orthopaedics) Serious injuries may require more resuscitation and result in higher mortalities
Pape et al., 2007 ¹⁵	<ul style="list-style-type: none"> Initial temporary external fixation (EF) n = 71 Early Intramedullary Nailing (IMN) n = 94 <p>Subgroups:</p> <ul style="list-style-type: none"> Stable n = 121 Borderline n = 44 	<p>EF vs. IMN:</p> <ul style="list-style-type: none"> EF group significantly more severely injured (RTS, ISS, head trauma score) ($p < 0.01$) No difference in post-operative complications (Controlling for different initial injury severity) <p>Subgroup analysis:</p> <ul style="list-style-type: none"> <i>Stable:</i> IMN group had shorter duration on ventilator than EF group ($p < 0.05$) <i>Borderline:</i> IMN group had higher incidence of ALI than EF (odds ratio 6.69) ($p < 0.05$) 	<ul style="list-style-type: none"> In stable patients, IMN produced better outcomes In borderline patients, temporary initial external fixation has better pulmonary outcomes
Tuttle et al., 2009 ¹⁶	<ul style="list-style-type: none"> Early Total Care (ETC) n = 42 Damage Control Orthopedics (DCO) n = 55 	<p>ETC vs. DCO:</p> <ul style="list-style-type: none"> No statistically significant differences in outcomes: ARDS, MOF, ICU & hospital LOS Initial EF had significantly shorter operative time and less blood loss than primary IMN ($p < 0.005$) 	<ul style="list-style-type: none"> Method of fracture fixation does not have major impact on incidence of systemic complications DCO has benefit of fracture stabilization with decreased operative burden (time, blood loss)
Scannell et al., 2010 ¹⁷	<ul style="list-style-type: none"> Primary Intramedullary Nailing (<24 hours) (IMN) n = 126 External Fixation converted to IM nail (DC-EF) n = 19 Skeletal Traction converted to IM nail (ST) n = 60 	<p>ST vs. IMN:</p> <ul style="list-style-type: none"> ST group significantly higher mean AIS-head/neck, ISS, lower RTS, greater BD, and lower mean GCS score ($p < 0.01$) ST group had significantly worse outcomes: MOF, Pneumonia, LOS, ICU LOS, MV days, and death ($p < 0.0002$) <p>ST vs. DC-EF:</p> <ul style="list-style-type: none"> No difference in outcomes: ARDS, MOF, PE, DVT, Pneumonia, ICU LOS, MV days, Death DC-EF group had significantly higher incidence of sepsis and longer LOS ($p < 0.05$) In borderline: no differences in outcomes. 	<ul style="list-style-type: none"> Worse outcomes between ST and IMN due to differences in severity of injuries between groups ST traction has lower incidence of sepsis and shorter LOS compared to DC-EF, but no difference in outcomes If patient is not already under general anesthesia for another procedure, ST is a safe option
Femoral Shaft Fracture & Associated Chest Injury			
O'Toole et al., 2009 ¹³	<ul style="list-style-type: none"> Primary reamed intramedullary nailing (IMN) n = 199 External fixation converted to IMN (DCO) n = 28 <p>Subgroups: (n = IMN/DCO)</p> <ul style="list-style-type: none"> ISS >17 n = 199/28 ISS >17 and thoracic AIS score >2 n = 151/24 ISS >28 and thoracic AIS score >2 n = 60/18 	<p>DCO vs. IMN</p> <ul style="list-style-type: none"> DCO group significantly more injured ($p < 0.05$) DCO group had higher lactate levels at all time points than IMN ($p < 0.05$) IMN group had 1.5–3.3% ARDS rate compared to 0% in DCO (n.s.) <p>Subgroup Analysis:</p> <ul style="list-style-type: none"> <i>ISS >17:</i> DCO group had significantly higher rate of death and longer ICU LOS than IMN ($p < 0.05$) <i>ISS >17 and thoracic AIS >2:</i> DCO group had significantly higher death rate and longer ICU LOS than IMN ($p < 0.05$) <i>ISS >28 and thoracic AIS >2:</i> DCO group had significantly higher death rate and longer ICU LOS than IMN ($p < 0.05$) 	<ul style="list-style-type: none"> DCO reserved for patients who do not respond well to aggressive resuscitation IMN method had a relatively low rate of ARDS and death as long as patients adequately resuscitated

ISS = Injury Severity Scale; GCS = Glasgow Coma Score; AIS = Abbreviated Injury Scale; ICU = Intensive Care Unit; LOS = Length Of Stay; RTS = Revised Trauma Score; ARDS = Adult Respiratory Distress Syndrome; MOF = Multiple Organ Failure; BD = Base Deficit; MV = Mechanical Ventilation; DVT = Deep Vein Thrombosis; n.s. = not statistically significant

IMN within 24 hours of injury.^{24, 25} Two studies did not find a statistically significant difference between early or delayed IMN in terms of days on ventilation, ICU LOS, hospital LOS,²⁶ or discharge GCS,²³ but Starr et al.²⁶ did notice that a delay in femur stabilization was a statistically significant predictor of pulmonary complications. One study showed

that patients treated with IMN between 2–4 days of admission had lower rates of mortality and shorter hospital LOS compared to those treated within 24 hours or after four days of admission,²² but these results were not statistically significant. Another study, however, observed a statistically significant increase in complications and incidence of sepsis after

Table 3. Timing to Definitive Fixation in the Borderline Patient

Author, Year	Comparison	Criteria Met Before Conversion	Time to Definitive Fixation	Relevant Results	Conclusions
Scalea et al., 2000 ⁸	<ul style="list-style-type: none"> External Fixation (EF) n = 43 Intramedullary nailing (IMN) n = 281 	<ul style="list-style-type: none"> “normalized” lactate (median time to normalization: 28 hours) *normal value not stated Mean cardiac index: 5.9 L/min per m² opening ICP: 22 mmHg 	4 days (median)	<ul style="list-style-type: none"> ICU-LOS: 11.0 days (median) for EF group, 8.0 days for IMN group Hospital LOS: 17.5 days (median) for EF group, 5.7 days for IMN group (<i>p</i> = 0.001) Deaths: 9% of EF group 	<ul style="list-style-type: none"> Patients treated with EF tended to be more seriously injured Deaths in the EF group were not secondary to fracture management selected (due to serious irreversible brain injury, or organ failure)
Harwood et al., 2006 ⁹	<ul style="list-style-type: none"> Initial External Fixation (DCO) n = 98 Intramedullary nailing (IMN) n = 75 	Senior surgeon’s discretion based on: <ul style="list-style-type: none"> hemodynamic stability local soft-tissue status presence of systemic complications logistic availability of staff and operating rooms 	Subgroups of DCO: <7 days (n = 31) 7–14 days (n = 28) >14 days (n = 52)	<ul style="list-style-type: none"> Significantly more pin-site contamination after 14 days compared to before 14 days 	<ul style="list-style-type: none"> Pin-site contamination did not have clinical consequence Earlier conversion to IMN can reduce chance of contamination, but not worth risking patient stability
Scannell et al., 2010 ¹⁷	<ul style="list-style-type: none"> Primary Intramedullary Nailing (<24 hours) (IMN) n = 126 External Fixation converted to IM nail (DC-EF) n = 19 Skeletal Traction converted to IM nail (ST) n = 60 	Not stated	DC-EF group: 5.04 days (mean) ST group: 4.08 days (mean)	<ul style="list-style-type: none"> No significant difference in mean time to definitive fixation b/n ST and DC-EF groups No difference in outcomes: ARDS, MOF, PE, DVT, Pneumonia, ICU LOS, MV days, Death DC-EF group had significantly higher incidence of sepsis and longer LOS 	<ul style="list-style-type: none"> Both DC-EF and ST treated patients were converted to definitive fixation within a similar time period of 4–5 days However, the criteria for conversion were not stated

ICP = Intracranial Pressure; ICU = Intensive Care Unit; LOS = Length of Stay; ARDS = Acute Respiratory Distress Syndrome; MOF = Multiple Organ Failure; PE = Pulmonary Embolism; DVT = Deep Vein Thrombosis; MV = Mechanical Ventilator

delayed IMN compared to IMN.¹¹ One study observed occurrence of intraoperative hypotension based on time to operative fixation and found a statistically significant eight-fold increase in risk of hypotension if the fixation procedure happened within two hours of admission compared to after 24 hours.²⁷ However, no statistically significant difference in mortality was observed between patients who did or did not experience intraoperative hypotension. In these studies, definitive fixation proceeded based on criteria similar to those mentioned above^{11, 25} or at the neurosurgeon’s discretion.^{26, 27}

Physiological Indicator of Patient Stability

There was one study that compared outcomes based on early (<24 hours of injury) definitive fixation in resuscitated and incompletely resuscitated multiply injured patients. Crowl et al.²⁸ observed that patients with femoral shaft fractures treated with early definitive fixation without adequate resuscitation had a significantly higher rate of complications (50%) compared to patients who were treated after complete resuscitation (20%) (*p* < 0.01). The incompletely resuscitated patients also suffered from significantly more infections and incurred significantly higher hospital costs compared to their adequately resuscitated counterparts.

Discussion

Identifying the Borderline Patient

Several studies have picked out patient profiles that tend to have complications after early IMN. Pape et al.⁵ was one of the first authors to challenge the ETC approach when he noticed that patients with a femoral shaft fracture and thoracic injury had a significantly higher incidence of ARDS after early IMN compared to a similarly treated group without thoracic injuries. Within the group with associated thoracic injuries, the incidence of ARDS was higher after early IMN compared to delayed IMN, but the difference did not reach significance. Zalavras et al.¹² also identified thoracic injuries as a risk factor for respiratory failure. Both Morshed et al.¹⁰ and Nahm et al.¹¹ found an increased risk of complications in patients with severe abdominal injuries, which further diversified the borderline patient profile. The authors from the shock trauma center in Baltimore stated that their DCO patients represented a small percentage of the femoral shaft fractures that they treat, and that these patients tended to be more severely injured and unstable.^{8, 13}

It is important to identify borderline patients, because they are a group of patients that tend to have poorer outcomes

Table 4. Timing to Definitive Fixation for Femoral Shaft Fracture and Concomitant Chest Injury

Author, Year	Comparison	Criteria Met Before Definitive Fixation	Time to Definitive Fixation	Relevant Results	Conclusions
Pape et al., 1993 ⁵	<ul style="list-style-type: none"> Thoracic trauma (AIS thorax ≥ 2) + IMN <24 hours (TI) n = 24 Thoracic trauma (AIS thorax ≥ 2) + IMN >24 hours (TII) n = 26 No thoracic trauma (AIS thorax <2) + IMN <24 hours (NI) n = 33 No thoracic trauma (AIS thorax <2) + IMN >24 hours (NI) n = 23 	Not stated	<ul style="list-style-type: none"> TI & NI = <24 hours after trauma TII & NII = >24 hours after trauma 	<ul style="list-style-type: none"> Duration CMV: NII longer than NI ($p < 0.05$) Total duration of ventilation: NII longer than NI ($p < 0.05$) ICU stay: NII longer than NI ($p < 0.05$) Incidence of ARDS: TI had greater incidence than NI ($p < 0.05$) and TII (n.s.) Mortality: TI had highest incidence (n.s.) 	<ul style="list-style-type: none"> If AIS thorax <2, IMN within 24 hours reduces duration of ventilation, CMV, and length of ICU stay compared to IMN after 24 hours If AIS thorax ≥ 2, IMN within 24 hours has greater risk of ARDS compared to AIS thorax <2 treated in same time frame AIS thorax ≥ 2, IMN within 24 hours has higher incidence of ARDS and mortality than IMN after 24 hours, but not statistically significant
Fakhry et al., 1994 ²²	<p>Management of femoral fracture (n = ISS <15/ISS ≥ 15):</p> <ul style="list-style-type: none"> Group I: non-surgical n = 665/200 Group II: surgery within one day of admission n = 965/212 Group III: surgery 2–4 days after admission n = 387/55 Group IV: surgery >4 days after admission n = 256/65 <p>Subanalysis:</p> <ul style="list-style-type: none"> severe head injury (AIS ≥ 3) severe chest injury (AIS ≥ 3) 	Not stated	<p><u>ISS ≥ 15 and chest injury (AIS ≥ 3):</u></p> <ul style="list-style-type: none"> Group I: non-surgical n = 71 Group II: within one day of admission n = 69 Group III: 2–4 days of admission n = 19 Group IV: >4 days after admission n = 27 	<p><u>For ISS ≥ 15 and severe chest injury (AIS ≥ 3):</u></p> <p>Mortality:</p> <ul style="list-style-type: none"> Group I had significantly higher mortality compared to operative groups ($p < 0.001$) Group II had highest mortality compared to delayed surgery (n.s.) Hospital LOS increased with delay in surgery (n.s.) 	<ul style="list-style-type: none"> Femoral fractures treated within one day of admission has higher mortality rate than delayed, but this did not reach statistical significance However, increasingly delayed surgery was associated with longer hospital LOS
Boulanger et al., 1997 ¹⁹	<ul style="list-style-type: none"> Thoracic injury (AIS thorax ≥ 2) + early IMN ≤ 24 hours (TE) n = 68 Thoracic injury (AIS thorax ≥ 2) + late IMN >24 hours (TL) n = 15 No thoracic trauma (AIS thorax < 2) + early IMN ≤ 24 hours (NE) n = 57 No thoracic trauma (AIS thorax < 2) + IMN >24 hours (NL) n = 9 Case control group with AIS thorax ≥ 2 and ISS >16 without a femur fracture (T) n = 68 	Not stated	<ul style="list-style-type: none"> TE & NE = <24 hours after injury TE & NE = >24 hours after injury 	<ul style="list-style-type: none"> No difference in % survival, total hospital stay, total critical care days, % admitted to ICU, or duration of ventilation between TE, NE, and T No difference in incidence in ARDS, reported fat embolism, pneumonia, pulmonary embolism, or MOD between TE, NE, and T groups 	<ul style="list-style-type: none"> Early IMN within 24 hours of injury presence of blunt thoracic injury (AIS ≥ 2) is not additionally detrimental to patient outcomes compared to either non-thoracic injury patients (AIS <2) with femur fractures or thoracic injury patients (AIS ≥ 2) without femur fractures Study could not compare TE vs. TL because TL group was too small
Brundage et al., 2002 ²³	<p>Severely injured patients with coexistent chest (Chest AIS ≥ 2) or head (Head AIS ≥ 2) injuries with IM fixation occurring:</p> <ul style="list-style-type: none"> <24 hours (I) n = 867 24–48 hours (II) n = 155 48–120 hours (III) n = 37 >120 hours (IV) n = 22 Nonoperative fixation (V) n = 281 	Not stated	<p><u>Chest AIS ≥ 2:</u></p> <ul style="list-style-type: none"> I: <24 hours n = 186 II: 24–48 hours n = 43 III: 48–120 hours n = 14 IV: >120 hours n = 8 V: Nonoperative n = 77 	<p><u>For patients with chest trauma (Chest AIS ≥ 2):</u></p> <ul style="list-style-type: none"> Mortality: Groups I–IV no statistical difference, Group V had highest mortality rate (40%) ARDS: Significantly higher incidence in Group III (64%) compared to Group I (12%) ($p < 0.0001$) Mean hospital and ICU LOS: longer times in Group III vs Group I (p value not reported) 	<ul style="list-style-type: none"> No statistically different rates of mortality as function of time to operative management ARDS incidence was significantly lower in patients with chest trauma treated <24 hours compared to 48–120 hours

Table 4. Timing to Definitive Fixation for Femoral Shaft Fracture and Concomitant Chest Injury (Continued)

Author, Year	Comparison	Criteria Met Before Definitive Fixation	Time to Definitive Fixation	Relevant Results	Conclusions
Handolin et al., 2004 ²⁰	Chest injured patients (Thoracic AIS ≥ 3) with: • Fracture + IMN n = 27 • No fracture n = 34	Not stated	Within 24 hours of injury	<ul style="list-style-type: none"> Length of ventilator treatment: no difference between groups ARDS, pneumonia, and MOF: no correlation to IMN shown 	<ul style="list-style-type: none"> No observed immediate harmful effects of femoral fracture treated with IMN within 24 hours of injury in patients with associated chest injury Included femoral and tibial shaft fractures, so isolating effect of femoral IM nailing is not possible
Weninger et al., 2007 ²¹	<ul style="list-style-type: none"> Severe thoracic trauma (Thoracic AIS ≥ 3) and early unreamed IMN (Study) n = 45 Severe thoracic injury (Thoracic AIS ≥ 3) without lower extremity fracture (Control) n = 107 	Upon arrival or within one hour after admission: Stable hemodynamic condition (systolic BP >90 mmHg) Stable respiratory condition	Within six hours after admission	No statistically significant differences between groups for: <ul style="list-style-type: none"> duration of ventilation duration of ICU stay rate of pneumonia rate of organ insufficiencies rate of MOFS rate of morbidity 	<ul style="list-style-type: none"> Unreamed IM nailing within six hours after admission did not produce worse outcomes than thoracic injury patients without femoral fractures
O'Toole et al., 2009 ¹³	<ul style="list-style-type: none"> Primary reamed intramedullary nailing (IMN) n = 199 External fixation converted to IMN (DCO) n = 28 Subgroups: (n = IMN/DCO) <ul style="list-style-type: none"> ISS >17 n = 199/28 ISS >17 and thoracic AIS score >2 n = 151/24 ISS >28 and thoracic AIS score > 2 n = 60/18 	<ul style="list-style-type: none"> Lactate trending toward 2.5 mmol/L or less optimized ventilatory and hemodynamic parameters 	IMN: 14.0 hours (mean time from admission) DCO: time to conversion to IM not reported	DCO vs. IMN <ul style="list-style-type: none"> DCO group significantly more injured ($p < 0.05$) DCO group had higher lactate levels at all time points than IMN ($p < 0.05$) IMN group had 1.5–3.3% ARDS rate compared to 0% in DCO (n.s.) Subgroup Analysis: <ul style="list-style-type: none"> ISS >17: DCO group had significantly higher rate of death and longer ICU LOS than IMN ($p < 0.05$) ISS >17 and thoracic AIS >2: DCO group had significantly higher death rate and longer ICU LOS than IMN ($p < 0.05$) ISS >28 and thoracic AIS >2: DCO group had significantly higher death rate and longer ICU LOS than IMN ($p < 0.05$) 	<ul style="list-style-type: none"> Definitive fixation within 24 hours in resuscitated patients has better outcomes than DCO approach IMN was not performed in emergent manner since mean time was 14.0 hours from admission
Nahm et al., 2011 ¹¹	For patients with associated injuries to chest (minor chest AIS <3; severe chest AIS ≥ 3) or head (minor GCS >8; severe ≤ 8) receiving either: • Definitive treatment <24 hours of injury (Early) • Definitive treatment >24 hours of injury (Delayed)	No formal protocol Resuscitation gauged by: • pH • Base deficit • lactate • ICP monitor for severe head injuries	<u>Patients with minor chest injury (AIS <3):</u> <ul style="list-style-type: none"> Early: <24 hours of injury n = 37 Delayed: >24 hours of injury n = 12 <u>Patients with severe chest injury (AIS ≥ 3):</u> <ul style="list-style-type: none"> Early: <24 hours of injury n = 122 Delayed: >24 hours of injury n = 49 	<u>For patients with chest injury:</u> <ul style="list-style-type: none"> more complications observed for delayed group vs. early group ($p < 0.0001$) odds ratio for developing pulmonary complications: surgical delay = 1.9 compared to early treatment ($p = 0.04$) <u>For patients with severe chest injuries:</u> <ul style="list-style-type: none"> Sepsis: Early group (2.5%) had lower incidence than delayed (10.2%) ($p = 0.044$) odds ratio for developing complications: surgical delay = 2.4 compared to early treatment ($p = 0.009$) 	<ul style="list-style-type: none"> Delayed definitive treatment beyond 24 hours doubles chance of developing pulmonary complications in patients with chest injuries Delayed definitive treatment beyond 24 hours showed greater incidence of sepsis in patients with severe chest injuries

AIS = Abbreviated Injury Scale; CMV = Controlled Mechanical Ventilation; ICU = Intensive Care Unit; ARDS = Acute Respiratory Distress Syndrome; ISS = Injury Severity Score; MOD = Multiple Organ Dysfunction; LOS = Length of Stay; MOF = Multiple Organ Failure; BP = Blood Pressure; MOFS = Multiple Organ Failure Syndrome; ICP = Intracranial Pressure; n.s. = not statistically significant

with the standard of treatment for femoral shaft fractures. It is also important to not include everyone as a borderline patient, as several authors have pointed out that DCO was

not intended to be generalized for every patient with femoral shaft fractures and multiple injuries, but rather a subset of patients who may be physiologically overwhelmed by

Table 5. Timing to Definitive Fixation for Femoral Shaft Fracture and Concomitant Head Injury

Author, Year	Comparison	Criteria Met Before Definitive Fixation	Time to Definitive Fixation	Relevant Results	Conclusions
Fakhry et al., 1994 ²²	Management of femoral fracture (n = ISS <15/ISS ≥15): <ul style="list-style-type: none"> Group I: non-surgical n = 665/200 Group II: surgery within one day of admission n = 965/212 Group III: surgery 2–4 days after admission n = 387/55 Group IV: surgery >4 days after admission n = 256/65 Subanalysis: <ul style="list-style-type: none"> severe head injury (AIS ≥3) severe chest injury (AIS ≥3) 	Not stated	<u>ISS ≥15 and head injury AIS ≥3:</u> <ul style="list-style-type: none"> Group I: non-surgical n = 82 Group II: within one day of admission n = 59 Group III: 2–4 days of admission n = 14 Group IV: >4 days after admission n = 14 	<u>For ISS ≥15 and severe head injury (AIS ≥3):</u> Mortality: <ul style="list-style-type: none"> Group I had significantly higher mortality compared to operative groups (<i>p</i> < 0.02) Groups II and IV showed higher mortality than Group III (n.s.) Hospital LOS lowest for patients operated on between 2–4 days (n.s.) 	<ul style="list-style-type: none"> Femoral fractures treated between 2–4 days suffered less mortality and shorter LOS, but not statistically significant
McKee et al., 1997 ²⁴	Femur Fracture with concomitant severe head injury (AIS head ≥3) (Study) n = 46 Matched severe head injury patients without femur fractures (Control) n = 99	During operative procedure: <ul style="list-style-type: none"> adequate CPP (minimum 70–80 mmHg) adequate oxygenation (minimum PaO₂ 80 mmHg) Patients with admitting GCS ≤7: ICP at or below 20–25 mmHg 	<24 hours (for 83% of study group)	<ul style="list-style-type: none"> Mortality: no difference between groups Hospital or ICU LOS: no difference between groups Neuropsychological testing: no difference between groups 	<ul style="list-style-type: none"> No demonstration of adverse effect of femoral fracture with early definitive fixation for patients with severe head injuries
Townsend et al., 1998 ²⁷	In patients with coexistent severe head injury (GCS ≤8), timing to operative fixation: <ul style="list-style-type: none"> 0–2 hours n = 22 2.01–12 hours n = 24 12.01–24 hours n = 3 24.01–244.0 hours n = 12 	Clearance by trauma surgeon and neurosurgeon	Intraoperative hypotension: <ul style="list-style-type: none"> eight-fold increase in risk if fixation occurs <2 hours of admission compared to after 24 hours (<i>p</i> < 0.007) four-fold increase in risk if fixation occurs within 2–24 hours compared to after 24 hours (<i>p</i> < 0.007) No statistically significant difference in mortality between patients with intraoperative hypotension and patients without intraoperative hypotension 	<ul style="list-style-type: none"> Risk of intraoperative hypotension can be 8x higher for patients with femoral fixation within two hours and 4x higher for patients with femoral fixation within 2–24 hours compared to patients with femoral fixation after 24 hours Intraoperative hypotension not associated with increased mortality 	<ul style="list-style-type: none"> No statistically different rates of mortality as function of time to operative management ARDS incidence was significantly lower in patients with chest trauma treated <24 hours compared to 48–120 hours
Starr et al., 1998 ²⁶	<ul style="list-style-type: none"> Severe head injuries (GCS ≤8) + fixation <24 hours (I) n = 9 Severe head injury (GCS ≤8) + fixation >24 hours (III) n = 5 Minor head injury (GCS >8) + fixation <24 hours (II) n = 6 Minor head injury (GCS >8) + fixation >24 hours (IV) n = 12 	On call neurosurgeon's discretion	I: 1 day II: 1 day III: 6 days IV: 7.44 days	No statistically significant differences between early and delayed fixation for neither severe nor minor head injuries: <ul style="list-style-type: none"> Days on ventilation Days in ICU Days in hospital Predictors of pulmonary complications: <ul style="list-style-type: none"> delay in femur stabilization >24 hours (<i>p</i> = 0.0042) severity of chest AIS (<i>p</i> = 0.0057) severity of head AIS (<i>p</i> = 0.0133) 	<ul style="list-style-type: none"> Delay in femur stabilization is a strong predictor of pulmonary complications No significant difference in length of stay found between groups Small sample size limits the study

Table 5. Timing to Definitive Fixation for Femoral Shaft Fracture and Concomitant Head Injury (Continued)

Author, Year	Comparison	Criteria Met Before Definitive Fixation	Time to Definitive Fixation	Relevant Results	Conclusions
Brundage et al. 2002 ²³	Severely injured patients with coexistent chest (Chest AIS ≥ 2) or head (Head AIS ≥ 2) injuries with IM fixation occurring: <ul style="list-style-type: none"> • <24 hours (I) n = 867 • 24–48 hours (II) n = 155 • 48–120 hours (III) n = 37 • >120 hours (IV) n = 22 • Nonoperative fixation (V) n = 281 	Not stated	Head AIS ≥ 2 : <ul style="list-style-type: none"> • I: <24 hours n = 283 • II: 24–48 hours n = 65 • III: 48–120 hours n = 17 • IV: >120 hours n = 13 • V: Nonoperative n = 133 	For patients with head trauma (Head AIS ≥ 2): <ul style="list-style-type: none"> • Discharge GCS: no statistically significant difference between Groups I–IV, but group V had significantly lower score than other groups ($p < 0.05$) 	<ul style="list-style-type: none"> • No statistically significant difference in neurological outcome based on time of definitive fixation
Nau et al., 2003 ²⁵	Multiple-injury patients with coexistent combined head and chest injury (head and chest AIS ≥ 2): <ul style="list-style-type: none"> • with femoral shaft fracture (study) n = 28 • without femoral shaft fracture (control) n = 120 	<ul style="list-style-type: none"> • Hemodynamic stability • Respiratory stability Both achieved within one hour of admission and remaining stable for following three hours after admission	Study group: within 24 hours of injury	No statistically significant difference between groups: <ul style="list-style-type: none"> • Mortality • Length of ICU stay • Ventilation time • GOS 	<ul style="list-style-type: none"> • No statistically significant difference in outcome between patients treated with IM nail within 24 hours of injury after hemodynamic and respiratory stability achieved compared to patients with chest and head injury without femoral fracture
Nahm et al., 2011 ¹¹	For patients with associated injuries to chest (minor chest AIS <3; severe chest AIS ≥ 3) or head (minor GCS >8; severe ≤ 8) receiving either: <ul style="list-style-type: none"> • Definitive treatment <24 hours of injury (Early) • Definitive treatment >24 hours of injury (Delayed) 	No formal protocol Resuscitation gauged by: <ul style="list-style-type: none"> • pH • Base deficit • lactate • ICP monitor for severe head injuries 	Patients with minor head injury (GCS ≥ 8): <ul style="list-style-type: none"> • Early: <24 hours of injury n = 155 • Delayed: >24 hours of injury n = 27 Patients with severe head injury (GCS ≤ 8): <ul style="list-style-type: none"> • Early: < 24 hours of injury n = 44 • Delayed: >24 hours of injury n = 22 	For patients with head injury: <ul style="list-style-type: none"> • more complications observed for delayed group vs. early group ($p < 0.001$) For patients with minor head injury: <ul style="list-style-type: none"> • more complications observed for delayed group vs. early group ($p = 0.002$) For patients with severe head injuries: <ul style="list-style-type: none"> • Sepsis: Early group (4.5%) had lower incidence than delayed (22.7%) ($p = 0.037$) 	<ul style="list-style-type: none"> • More complications observed for delayed definitive treatment beyond 24 hours in both minor and severe head injured patients • Delayed definitive treatment beyond 24 hours showed greater incidence of sepsis in patients with severe head injuries

ISS = Injury Severity Scale; AIS = Abbreviated Injury Scale; LOS = Length of Stay; CPP = Cerebral Perfusion Pressure; GCS = Glasgow Coma Score; ICP = Intracranial Pressure; ICU = Intensive Care Unit; GOS = Glasgow Outcome Score

another stimulus.^{1, 8, 13} To our knowledge there has not been a sensitivity or specificity analysis of the characteristics presented here to determine the likelihood of a borderline patient suffering pulmonary complications if treated with early IMN. However, they are included in our practice guidelines (Table 7) to help trauma and orthopaedic teams identify potential borderline patients.

Provisional Stabilization of Femoral Shaft Fracture

Patient outcome after provisional stabilization followed by conversion to definitive IMN relative to early IMN varies. In all of the studies comparing provisional stabilization and early IMN, the patients who were treated with provisional stabilization, whether by EF or ST, were significantly more severely injured than the early IMN patients.^{8, 13, 15–17} This difference may have contributed to the longer LOS and higher incidence of mortality found in the Scalea et al.,⁸

Scannell et al.,¹⁷ and O’Toole et al.¹³ studies. Scalea⁸ also mentioned that the deaths in their study were not secondary to the fracture management selected, but rather the initial injuries sustained. The prospective randomized intervention trial by Pape et al.¹⁵ showed a 6.69 fold increase in odds of developing ALI for borderline patients treated with early IMN instead of provisional EF, which gives strong evidence in favor of initial temporary EF in the borderline patient population. Provisional EF has a significantly shorter operative time and blood loss in the initial procedure compared to IMN, which reduces the operative burden for the vulnerable borderline patient.¹⁶ This is also supported by evidence that the DCO method induces a significantly lower systemic immune response compared to early IMN.⁹ There were no statistically significant differences in incidence of complications between the DCO and IMN groups in the Tuttle et al.¹⁶ study, but the groups represented two different time periods.

Table 6. Physiological Indicators for Definitive Fixation in Multiply Injured Patients

Author, Year	Comparison	Criteria Met Before Definitive Fixation	Time to Definitive Fixation	Relevant Results	Conclusions
Crowl et al., 2000 ²⁸	IM fixation within 24 hours of injury with: • Complete resuscitation (lactate <2.5 mmol/L) (Group I) n = 27 • Incomplete resuscitation (lactate >2.5 mmol/L) (Group II) n = 20	• Lactate <2.5 mmol/L • Systolic BP >100 mmHg • Heart rate <120 bpm • urine output ≥1 ml/kg per hour	Group I and II: within 24 hours of injuries	<ul style="list-style-type: none"> • Lactate at admission: Group II had higher levels than Group I ($p < 0.01$) • Lactate before surgery: Group II had higher levels than Group I ($p < 0.01$) • Time to correct lactate levels: Group II took significantly longer (16.8 hours) than Group I (8 hours) ($p < 0.05$) • Complications: Group II had significantly higher rate of complications (50%) than Group I (20%) ($p < 0.01$) • ISS >18: Group II had significantly more complications than Group I ($p < 0.05$) • Infectious complications: Group II had significantly more infections (72%) than Group I (28%) ($p < 0.01$) • Days on ventilator: no significant difference between groups • Hospital cost: Group II had significantly higher costs (\$53,540) compared with Group I (\$30,553) ($p < 0.001$) 	<ul style="list-style-type: none"> • Patients with uncorrected occult hypoperfusion before early IM fixation have increased incidence of postoperative complications, took longer to correct lactate levels, and had higher hospital costs

BP = Blood Pressure; ISS = Injury Severity Score

There is a possibility that the DCO era also benefited from advances in other resuscitation techniques that could have affected the results. This kind of effect was seen in Pape et al.’s²⁹ study that analyzed outcomes over time as their trauma center changed practice patterns from predominantly ETC to DCO over a period of 20 years. Incidence of post-operative complications decreased in all treatment methods over time, although incidence of ARDS was still higher in primary IMN treated patients than DCO treated patients in the most recent time period analyzed.

Only one study addressed provisional stabilization of femoral shaft fractures in patients with concomitant severe chest injury. The results suggested that DCO was reserved for the patients that did not respond to aggressive resuscitation, while the patients that were resuscitated quickly were treated with early IM nailing and went on to have better outcomes.¹³ The difference in patient ability to recover from initial trauma may have contributed to worse outcomes in the DCO group. It is also difficult to predict how these more severely injured patients would have fared with early definitive IM nailing.

Scannell et al.¹⁷ presented skeletal traction as an alternative or complement to external fixation. When compared to the early IMN treated group, the ST group was more seriously injured and suffered significantly worse outcomes, similar to DCO outcomes in the other studies. Relative to the DC-EF group, there were no differences in several outcome measures. However, the ST group had significantly lower incidence of sepsis and shorter overall LOS compared to the DC-EF group overall, though not in borderline patients. ST is easier to apply compared to EF, and there is no need for general anesthesia, unlike EF. However, the logistics of

implementing ST such as patient portability and patient mobility may be a concern in other settings.

Provisional stabilization is an important step in the initial management of multiply injured patients with femoral shaft fractures. In borderline patients, initial temporary external fixation may reduce the operative burden early on until they are physiologically stable enough for an IMN procedure. In patients with concomitant chest injuries, the DCO method may best serve the patients that have trouble being resuscitated quickly, since there is evidence that early IMN may yield better outcomes. There is no evidence in the literature that addresses provisional stabilization in patients with concomitant head injuries. Skeletal traction could be an alternative method to external fixation if the patient is not already under general anesthesia for another procedure. In any situation where provisional stabilization is utilized, the patient is most likely severely injured and susceptible to complications independent of the treatment modality used.

Timing of Definitive Fixation — Borderline Patient

After provisional stabilization of the femoral shaft fracture in a borderline patient, the next step is determining when the patient is ready for conversion to definitive fixation. Studies have reported times to conversion that were within one week of the initial procedure.^{8, 17} Only Scalea et al.⁸ reported physiologic criteria that were also met before conversion, which included a normalized lactate level that was not specified and a cardiac index value. Harwood et al.¹⁸ stated that conversion to IMN from EF proceeded at the senior surgeon’s discretion. Although, these authors found an increase in pin-site contaminations on patients who were converted to IMN after 14 days, they reported that these

Table 7. Practice Guidelines for Femoral Shaft Fractures in the Multiply Injured Patient

Borderline Patient	Concomitant Chest Injury	Concomitant Head Injury
I. Identification of Patient Subgroups		
<p>Description (modified from Pape et al.¹⁴):</p> <ul style="list-style-type: none"> • Polytrauma + ISS >20 and additional thoracic trauma (AIS >2) • Polytrauma with abdominal/pelvic trauma (> Moore 3, AIS ≥3*) and hemodynamic shock (initial BP <90 mmHg) • ISS 40 or above in the absence of additional thoracic injury • Radiographic finding of bilateral lung contusion • Initial mean pulmonary arterial pressure >24 mmHg • High presenting lactate level (~6.5 mmol/L)* • Multiple IMN procedures at one time* 	<p>Description:</p> <ul style="list-style-type: none"> • AIS chest/thorax ≥2 	<p>Description:</p> <ul style="list-style-type: none"> • AIS head ≥2 • GCS ≤8
II. Provisional Stabilization		
<p>Evidence:</p> <ul style="list-style-type: none"> • Evidence of lower risk of acute lung injury with provisional EF compared to early IMN¹⁵ and decreased operative burden¹⁶ • Evidence of comparable outcomes between provisional ST and EF, but lower risk of sepsis and no need for general anesthesia¹⁷ • Evidence of greater injury severity and worse outcomes in patients treated with EF or ST compared to early IMN candidates^{8, 15-17} 	<p>Evidence:</p> <ul style="list-style-type: none"> • Evidence of greater injury severity and worse outcomes in patients treated with provisional EF compared to adequately resuscitated patients treated with early IMN¹³ 	<p>Evidence:</p> <ul style="list-style-type: none"> • No literature supported evidence found
<p>Recommendation:</p> <ul style="list-style-type: none"> • Skeletal traction pin placed upon admission • Consider external fixation if patient is under general anesthesia for another procedure 	<p>Recommendation:</p> <ul style="list-style-type: none"> • Skeletal traction pin placed upon admission • For patients who do not respond quickly to resuscitation, consider external fixation if patient is already under general anesthesia 	<p>Recommendation:</p> <ul style="list-style-type: none"> • Skeletal traction pin placed upon admission
III. Timing to Definitive Fixation		
<p>Evidence:</p> <ul style="list-style-type: none"> • Reported conversion times from temporary stabilization to definitive IM nail between 4–5 days in the presence of adequate cardiopulmonary resuscitation^{8, 17} • Evidence of higher incidence of pin-site contamination without clinical consequence after conversion to definitive IMN past 14 days⁹ 	<p>Evidence:</p> <ul style="list-style-type: none"> • No evidence of worse outcomes due to presence of femoral shaft fractures treated with IMN <24 hours of injury in chest-injured patients¹⁹⁻²¹ • Evidence of worse outcomes with early compared to delayed definitive fixation, but may have analyzed borderline patient⁵ or failed to show statistical significance²² • Evidence of comparable mortality rate²³ and lower rate of pulmonary complications^{11, 23} with early IMN (<24 hours of injury) compared to delayed • EAST guidelines reported no difference in complications or hospital LOS between definitive treatment before and after 48 hours of injury based on Class II and III data³⁰ 	<p>Evidence:</p> <ul style="list-style-type: none"> • Evidence of comparable outcomes between head-injured patients with and without femoral shaft fracture^{24, 25} • Evidence of comparable outcomes between early (<24 hours) and delayed fixation^{23, 26} • Evidence of increased complications and rate of sepsis after definitive fixation >24 hours¹¹ • Evidence of eight-fold increased risk of intraoperative hypotension during IMN within two hours of injury²⁷ • Not statistically significant trend of lower mortality rate and shorter hospital LOS after definitive fixation between 2–4 days of admission compared to earlier or later treatment²² • EAST guidelines reported no difference in complications or hospital length of stay between definitive treatment before and after 48 hours of injury in head-injured patients based on class II and III data³⁰
<p>Recommendation:</p> <ul style="list-style-type: none"> • If patient is temporarily stabilized, conversion to definitive IM nail should occur within one week, if patient health permits • Adequate resuscitation required: lactate <2.5 mmol/L in presence of hemodynamic and respiratory stability** 	<p>Recommendation:</p> <ul style="list-style-type: none"> • Definitive fixation by IMN within 24 hours of injury, emergent treatment not required • Adequate resuscitation required: lactate <2.5 mmol/L, hemodynamic and respiratory stability** 	<p>Recommendation:</p> <ul style="list-style-type: none"> • Definitive fixation by IMN within 24 hours of injury, but emergent treatment within two hours of admission not recommended • Adequate resuscitation required: lactate <2.5 mmol/L, hemodynamic and respiratory stability** • Monitor ICP intraoperatively to maintain at or below 20–25 mmHg or as per neurosurgery

*Author added

**Resuscitation guidelines based on evidence of increased complications, infections, and hospital costs after early definitive fixation in incompletely resuscitated patients compared to completely resuscitated patients.²⁸

ISS = Injury Severity Scale score; AIS = abbreviated injury scale; BP = blood pressure; GCS = Glasgow Coma Score; EAST = Eastern Association of the Surgery of Trauma; ICP = Intracranial Pressure

contaminations were of no clinical consequence and warned against premature conversion.

Timing of Definitive Fixation — Concomitant Chest Injury

The reviewed studies provided conflicting evidence for the best timing of definitive fixation in non-borderline patients with a concomitant femoral fracture and chest injury. Multiple studies showed that among patients with chest injuries, there were no additional incurred risks because of the presence of a femoral shaft fracture and subsequent treatment with early IMN.^{19–21} Among these, Weninger et al.²¹ reported that the unreamed IMN procedure occurred within six hours of admission given that the patient was in stable hemodynamic (systolic blood pressure >90 mmHg) and respiratory condition within one hour after admission. However, these studies could not make comparisons between early IMN and delayed IMN because of their study design or small group size.¹⁹

The four studies that were able to compare early versus delayed IMN were split on the outcomes. Pape et al.¹⁴ found that patients with an AIS thorax score ≥ 2 and femoral shaft fracture treated with IMN within 24 hours of injury had a greater risk of ARDS compared to similarly injured patients treated with delayed IMN and compared to non-severe thoracic injured patients treated with IMN. However, only the difference between severe and non-severe thoracic injured patients was found to be statistically significant. Fakhry et al.²² observed that patients with severe chest injuries treated with definitive fixation within one day of admission trended toward higher rates of mortality than patients treated after one day, but this finding was complicated by evidence that delayed surgical treatment was associated with longer hospital stays. Neither of these results reached statistical significance. In contrast to these findings, Brundage et al.²³ did not find a statistically significant difference in mortality rates based on timing of operative management. These authors did find a significantly lower incidence of ARDS in chest-injured patients treated within 24 hours compared to between 48–120 hours. These results were supported by Nahm et al.¹¹ who observed a statistically significant two-fold increased risk of developing pulmonary complications and a significantly higher incidence of sepsis after delayed (>24 hours of injury) IMN treatment in chest-injured patients with a femoral shaft fracture. In their study, the authors reported that there was no formal protocol in place to determine when to proceed with IMN, but that resuscitation was gauged by pH, base deficit, lactate, and ICP monitor.

O'Toole et al.¹³ was the lone study that compared early IMN and DCO methods for chest-injured patients. Their findings support early, but not emergent, definitive fixation by IMN in this patient subpopulation unless they are not adequately resuscitated quickly, in which case they may be treated with DCO. The authors defined resuscitation by lac-

tate levels trending to <2.5 mmol/L in the presence of optimized ventilatory and hemodynamic parameters, which were not stated. The EAST (Eastern Association of the Surgery of Trauma) guidelines for femoral shaft fractures in polytrauma patients reported no difference in mortality, ARDS, mechanical ventilation requirements, ICU LOS, and hospital LOS with definitive treatment before and after 48 hours of injury based on class II and class III data.³⁰

The findings reported in this review generally echo those of the EAST guidelines, but add recent evidence supporting early IMN and provide physiological measures that can be used to help determine a patient's fitness for an IMN procedure.

Timing of Definitive Fixation — Concomitant Head Injury

Evidence for the best timing of definitive fixation in patients with a concomitant femoral fracture and head injury seems to favor early, but not emergent treatment. McKee et al.²⁴ observed that patients with head injuries (AIS ≥ 3) and concomitant femoral shaft fracture treated with reamed IM nailing within 24 hours of injury showed no difference in early mortality, LOS, or long-term neurological function compared to matched head injured patients without femoral fractures. Nau et al.²⁵ observed no statistically significant difference in mortality, length of ICU stay, ventilation time, nor Glasgow Outcome Score (GOS) between multiply injured patients with concomitant head and chest injuries with and without femoral shaft fractures, given respiratory and hemodynamic stability before the IMN procedure. These results suggest that the addition of a femoral shaft fracture with early treatment did not yield worse outcomes for patients with head injuries.

Fakhry et al.²² observed that patients with severe head injuries (AIS ≥ 3) who had their femoral shaft fracture definitively treated between 2–4 days trended towards lower mortality and shorter hospital LOS compared to those treated within one day or after four days, but differences did not reach statistical significance. Nahm et al.,¹¹ however, found a statistically significant difference in outcomes that favored early definitive fixation to delayed treatment in head-injured patients. Starr et al.²⁶ found no statistically significant differences between early and delayed fixation for neither minor (GCS >8) nor severe (GCS ≤ 8) head injuries, though their sample sizes were small. However, a delay in femur stabilization beyond 24 hours was found to be a strong predictor of pulmonary complications. Townsend et al.²⁷ found that definitive fixation of femoral shaft fractures in patients with severe head injuries (GCS ≤ 8) within two hours of admission was associated with an eight-fold increased risk of intraoperative hypotension compared to after 24 hours. Furthermore, operation between 2–24 hours was associated with a four-fold increased risk of hypotension compared to after 24 hours. This study was unique in that it analyzed

smaller time periods than 24-hour increments. However, the authors did not find an association between intraoperative hypotension and mortality.

The reviewed findings are mostly in line with the EAST guidelines, which report no difference in outcomes based on timing of definitive fixation.³⁰ However, the recent articles reviewed here may add evidence suggesting early definitive fixation may have clinical benefits over delayed fixation, as long as the patient is stabilized.

Physiological Indicator of Patient Stability

Although almost half of the studies stated some sort of criteria met before the surgeons proceeded with definitive fixation of femoral shaft fractures, few reported specific values. Crowl et al.,²⁸ however, were able to show that completely resuscitated patients with femoral shaft fractures treated with an IM nail within 24 hours of injury had fewer complications and lower hospital costs than those who were treated without adequate resuscitation. The study reported threshold values for lactate (<2.5 mmol/L), systolic BP (>100 mmHg), heart rate (<120 bpm), and urine output (>1 ml/kg per hour) to differentiate completely resuscitated patients from incompletely resuscitated ones. O'Toole et al.¹³ reported using a similar lactate threshold for patients undergoing a primary reamed IM nailing procedure, while Scalea et al.⁸ mentioned a "normalized" lactate criterion for their patients without giving a specific value. In further support of Crowl's study, a recent study by Grey et al.³¹ observed an increased requirement for inotropic support for patients who underwent femoral fracture fixation with preoperative lactate >2.5 and otherwise normal vital signs compared to those with preoperative lactate <2.5. Another potential marker for hypoperfusion is serum bicarbonate. Morshed et al.³² showed an association between IMN procedures performed in the setting of serum bicarbonate-defined hypoperfusion and pulmonary organ dysfunction in multiply-injured patients. Although the use of serum bicarbonate as a diagnostic of hypoperfusion has yet to be validated by another study, this study does provide further evidence that physiologic markers can help guide clinicians determine when to proceed with IMN in multiply injured patients.

Conclusion

Much of the literature has been concerned about the timing of definitive fixation of femoral shaft fractures in multiply injured patients. The debate over the ideal time to IMN continues, but few studies have analyzed results based on smaller time intervals than 24 hours. This time period could span from emergent treatment to treatment the next morning. There may be a smaller time interval than 24 hours when patient outcomes can begin to diverge. Recently, an increasing number of studies have reported physiological parameters used to determine patient stability for an IMN procedure. These parameters, such as lactate level, can be

complementary guiding factors in addition to concerns about time in the management of femoral shaft fractures in multiply injured patients.

Results of the reviewed studies were weighed with respective study designs and sample sizes to create practice guidelines for the initial treatment of femoral shaft fractures in the multiply injured patient intended for use at Temple University Hospital (Table 7). Although there was only one prospective randomized trial reviewed, the collective sample size of the studies gives a substantial amount of evidence for the approach we describe. Our guidelines generally agree with those put forth by EAST, but also serve as an update to their guidelines, which are now more than 10 years old. However, it should be noted that only articles written in English were included in this review, which excluded a large number of German studies that have contributed to the topic. We believe that there was enough evidence with North American patients to create a set of practice guidelines that could be implemented at our trauma center in Philadelphia.

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Training and Prolonged Performance of a Low Force Repetitive Task by Mature Rats Induced Detrimental Bone Remodeling, Cortical Porosity and Inflammation

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Abstract

We have shown that repetitive reaching and grasping leads to trabecular bone adaptation in young adult rats at moderate force loads. Our goal here was to assess forearm bone microarchitecture in mature rats performing a moderate level reaching and grasping task, with the hypothesis that bone quality would decrease. We examined radii of three groups of mature rats (14 months of age at onset of experiment): 1) rats that trained for 10 minutes/day for four weeks to perform a high repetition low force task, and then performed this task for two hours/day for 12 weeks (HRLF Mature); 2) age-matched rats that trained only and then rested for 12 weeks (TRLF + Rest); and 3) age-matched normal controls (NC Mature). TNF α and IL-1 β increased in distal and diaphyseal regions of TRLF + Rest and HRLF Mature bones, IL-6 increased in diaphyseal region of HRLF Mature bones, while IL-10 decreased in diaphyseal HRLF Mature bones. Micro-computed tomography analysis of TRLF + Rest and HRLF Mature bones showed that despite no loss in bone volume, significant anisotropic and structure model index changes were present in distal trabeculae. Their mid-cortical diaphyses also showed endosteal resorption, cortical thinning and increased porosity, indicative of reduced cortical bone quality, compared to NC Mature rats. Thus, repetitive reaching and grasping at constant moderate loading levels, leads to increased bone inflammatory cytokines, reduced trabecular bone quality without loss of bone volume, and decreased cortical bone quality, changes associated with increased fracture risk.

Introduction

According to the Bureau of Labor Statistics report titled “Nonfatal Occupational Injuries and Illnesses Requiring Days Away from Work, 2012,” work-related musculoskeletal disorders (WMSDs) account for 33% of lost workday injuries and illnesses in the US, and are estimated to cost over \$61.2 billion annually.¹ However, the mechanisms leading to pathophysiological tissue changes associated with WMSDs are incompletely understood. The 2010 National Manufac-

turing Agenda of the National Institute of Occupational Safety and Health cites the need for etiologic research in determining the contribution of biomechanical and biochemical mechanisms towards the development of tissue injury and musculoskeletal disorders.^{2,3} Recent government show increased risk of WMSDs of the upper extremities in people above 35 years of age.^{1,2} As the average age of the American workforce rapidly increases,⁴ due to economic realities in the United States (as well as world-wide), more WMSD cases are predicted, enhancing the need for understanding the effect of WMSD long-term on aging musculoskeletal tissues.

Hand and wrist injuries are prevalent in occupations requiring upper extremity repetitive tasks, and can be further aggravated by advancing age.^{5,6} Both acute and cyclical over-load of tissues can affect bone quality and morphology.^{7,8} Prolonged performance of repetitive tasks, dependent on the force load, repetition rate and duration of task, can either lead to bone adaptation or pathological bone changes.⁹ Prior work from our lab using our innovative rat model of WMSDs in which rats voluntarily perform an upper extremity repetitive reaching and grasping task, showed that forelimb bones undergo exposure-dependent increases in pro-inflammatory cytokines (e.g., IL-1 β and TNF- α), and greater bone resorptive changes and cartilage damage with higher force loads.⁹⁻¹¹ We have also observed enhanced inflammatory cytokine production in serum and tendons of mature rats performing a high repetition low force (HRLF) task,¹² compared to young adult rats performing the same task, as well as in serum of mature control rats compared to young adult control rats.¹³ In these studies, the mature rats were 14–18 months of age during the course of the experiment, while the young adults rats were 2.5–6.5 months of age). These serum changes were concomitant with enhanced task-induced degenerative changes in forelimb tendons in mature HRLF rats.¹² These results are consistent with other studies showing that aging mammals typically have increased IL-1 β and TNF- α in tissues and systemically, compared to young adult mammals, even in the absence of detectable tissue injury.^{14,15} These cytokines are known to stimulate osteoclast formation and to impair osteoblast differentiation.¹⁶⁻²⁰ We have already reported qualitative bone changes in young adults performing a high repetition low

force (HRLF) task for 12 weeks, but we have yet to examine bones of aging mature rats in our WMSD animal model.⁹

Aging is not only associated with decreased bone quality and mass,^{8, 21–25} but also with normal structural parameter changes²⁶ triggered by age-related hormonal and inflammatory changes.^{15, 27} The loading threshold required to initiate an osteogenic response is higher in aging bones than in younger bones.^{8, 25} Therefore, the effect of performing repetitive tasks on bone architecture needs further evaluation to assess if aging combined with performance of repetitive task for 12 weeks enhances bone inflammation, remodeling or degradation.

Thus, our aim here was to investigate the impact of WMSD on bones in aging (mature) non-menopausal female rats, as very little is known about WMSDs in an aging population. We favored a female rat model based on the higher prevalence of these disorders in women,²⁸ and for comparison to data from our past studies on young adult female rats, using this model. We hypothesized that low grade loading occurring during the initial training period of 10 minutes/day, five days/week, for four weeks (TRLF + Rest rats), would encourage bone formation and indicate potential adaptation or reduced resorption. We further hypothesized that performance of a high repetition low force (HRLF) task for two hours/day, three days/week for 12 weeks (HRLF Mature rats) would lead to bone changes indicative of degradation.

Materials and Methods

Overview

Using our innovative operant animal model of a repetitive upper limb reaching and handle-pulling task, we examined radii of three groups of mature female rats (14 months of age at onset of experiment): 1) rats that trained for 10 minutes/day for four weeks to perform a low force task, and then performed a high repetition low force task for two hours/day for 12 weeks (HRLF Mature); 2) age-matched rats that trained only and then rested for 12 weeks (TRLF + Rest); and 3) age-matched normal controls (NC Mature). We performed the following analyses: investigated pro-inflammatory cytokines in forelimb bones, and bone morphometric using micro-computerized tomography (microCT).

Animals

All experiments were approved by the Temple University Institutional Animal Care and Use Committee and were in compliance with NIH guidelines for humane care and use of laboratory animals. A total of 48 mature aging adult female Sprague-Dawley rats were used (14 months of age at onset of experiments; 18 months at completion). The rats were housed in a central animal facility in separate cages with a 12 hour light-dark cycle with free access to water and environmental enrichment toys. After the first week of acclimation, animals were randomly selected to NC Mature (n = 18), TRLF + Rest (n = 12), or HRLF Mature (n = 14) groups; rats

were yoked and age-matched throughout the experiment. There were also four food-restricted control rats used to confirm the validity of using free access to food rats (NC rats) as controls. TRLF + Rest and HRLF Mature rats were weight-matched as well. In addition to 45 mg food pellet rewards provided during training and task performance (a 1:1 mix of purified grain and banana flavored pellets, both from Bioserve, NJ, USA), all rats received Purina rat chow daily. Results were compared to age-matched NC Mature rats that received similar amounts of food reward pellets daily as TRLF + Rest and HRLF Mature rats, in addition to free access to Purina rat chow. Three additional rats had to be excluded, as one was euthanized before the completion of the experiment due to renal failure, another due to presence of palpable tumors, and one that died unexpectedly. To further reduce illness-related confounders, additional sentinel rats were examined for presence of viral infections as part of the regular veterinary care (no viruses or infections were detected).

Behavioral Task Apparatuses, Training and Task Performance

The behavioral apparatuses used were 16 custom-designed force apparatuses (Custom Medical Research Equipment, Glendora, NJ) that were integrated into an operant behavioral training system (Med Associates, Georgia, VT), as previously described and depicted.²⁹ Training and task performance were as described previously.⁹

Analysis of Bone Cytokines Using ELISA

To study bone inflammation, cohorts of animals were deeply anesthetized with 5% isoflurane in oxygen, blood collected by cardiac puncture using a 23-gauge needle, and euthanized using cardiac exsanguination. Forelimb bones were collected from subcohorts of animals: NC Mature (n = 14), TRLF + Rest (n = 8), HRLF Mature (n = 8), and four food-restricted only control rats. Soft tissue were removed from the bones, and then distal (carpal bones, epiphysis and metaphysis of the radius and ulna) and proximal (diaphysis of radius and ulna) bones were separated, flash-frozen, and homogenized separately to assess interleukin (IL)-1 β and tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6) and anti-inflammatory cytokine interleukin-10 (IL-10) using commercially available ELISA kits (BioSourceTM, Invitrogen Life Sciences, CA), as described previously.³⁰ Each sample was run in duplicate. ELISA data (pg cytokine protein) were normalized to total protein, determined using a bicinchoninic acid (BCA) protein assay kit (Thermo Scientific Pierce BCA Protein Assay).

MicroCT Imaging and Analysis

Rats were deeply anesthetized and blood collected as described above. They were perfused transcardially with 0.9% saline and then with 4% paraformaldehyde in 0.1 M PO₄ buffer (pH 7.4). Forelimb bones were collected and

cleaned of soft tissues from the dominant reach limbs of: NC Mature (n = 5), TRLF + Rest (n = 4) HRLF Mature (n = 6). The microarchitecture of radial trabecular bone at the distal metaphysis and the diaphysis cortical bone were investigated using a SkyScan 1172-12mPix high resolution cone-beam microCT scanner (Skyscan, Ltd, Antwerp, Belgium). First, collected forelimb bones were stored in 4% paraformaldehyde in 0.1 M PO₄ buffer. Twenty-four hours prior to microCT analysis, the bones were rinsed and immersed in phosphate buffered saline. Forelimb bones of food-restricted only rats (n = 4) were also analyzed in a separate study and used to confirm the validity of using free access to food rats (NC rats) as controls. The bones were scanned from the metacarpal bones of the wrist to mid-shaft using the following settings: air media wrapped in parafilm, x-ray source spot size of 300 nm, pixel size of 5.89 μm, Al 0.5 mm filter, voltage of 59 kV, current of 167 μA, rotation step of 0.40°, frame averaging of five. Each scan approximately took 45 minutes per bone. During reconstruction of the images (Skyscan NRecon), a ring artifact correction of 10, and a beam hardening correction of 60% were applied to all samples. The image slices were reconstructed using cone-beam reconstruction software based on the Feldkamp algorithm.

Using the Skyscan CT Analyzer (CTAn) software, two regions of interest (ROI) of the radius were delineated using a region of interest tool, and then binarized separately. The metaphyseal trabecular bone ROI was defined from 1.5 mm below the center of the distal growth plate and extending proximally for 1 mm (170 slices). The volume of interest (VOI) for the trabecular microarchitecture variables was defined by a consistent circle shape within a few pixels inside the endocortical margin. The cortical diaphyseal ROI was delineated from 5 mm below the distal growth plate and extending proximally from that side for 0.5 mm. The cortical VOI was defined by circling the outside of the cortical bone surface. The registered data sets were segmented into binary images. Because of a low noise and the relative good resolution of the data sets, we used simple global thresholding methods. For trabecular bone, an upper threshold of 255 (the maximum) and a lower threshold of 95 were used. For the cortical analysis, the upper threshold remained 255, but the lower threshold was increased to 125 to delineate each pixel as “bone” or non-bone. Despeckling was performed at a two-dimensional setting of 50 pixels, prior to two-dimensional (2D) and three-dimensional (3D) analyses of both ROIs. We also utilized the shrink-wrap option of the CTAn software to cover holes of more than 50 pixels for the cortical analysis, in order to eliminate larger arterial profiles from the analysis.

Trabecular morphometric traits were computed from binarized images using direct 3D techniques that do not rely on prior assumptions from the underlying structures. Trabecular bone volume per total volume (BV/TV), bone surface per bone volume (BS/BV), bone surface density (BS/TV), mean trabecular thickness (Tb.Th.), mean trabecular number (Tb.N.), and mean trabecular separation (Tb.Sp.)

were measured in 3D, along with degree of anisotropy (DA — indicator of mechanical strength) and structure model index (SMI — rods or plates architecture). Cortical morphometry was analyzed from obtained binarized images using 2D techniques. Total cross-sectional area inside the periosteal envelope (Tt.Ar.), cortical bone area (Ct.Ar.), Cortical area fraction (Ct.Ar./Tt.Ar.) and average cortical thickness (Ct.Th) were reported based on the Journal of Bone and Mineral Research guidelines.³¹ Additionally, we gathered data about cortical porosity (Ct.Po.) pore volume (Po.V.) and pore density volume (Po.Dn.), which can be indicators of microdamage and Haversian system remodeling. The person carrying out the microCT analyses was blinded to treatment.

Statistical Analyses

To determine differences between and among groups, one-way ANOVAs were performed for ELISA for cytokines and microCT data. To determine the effect of the dependent variables, for each ANOVA, the Bonferroni post-hoc method for multiple comparisons was used. Adjusted p-values are reported, and after adjustment, a p-value of <0.05 was considered statistically significant. A two-tailed Pearson's correlation test was used to compare cortical area (Ct.Ar.), bone volume (BV/TV) and cortical thickness (Ct.Th.) with the animal weights and estrogen level at euthanasia. Data are expressed as mean ± standard error of the mean (SEM). One-way ANOVA p-values are listed with the individual graphs.

Results

Inflammatory Cytokines Increased with Training and Task in Forelimb Bones

Significant changes in cytokines were observed in both distal and proximal forelimb bone regions. IL-1beta and TNF-alpha increased in distal forelimb bones of TRLF + Rest and HRLF Mature rats, compared to NC Mature rats (Fig. 1A, C), while IL-10 was reduced in HRLF Mature rats only (Fig. 1G). TNF-alpha, IL-1beta and IL-6 increased in proximal diaphysis of forelimbs bones of TRLF + Rest and HRLF Mature rats (Fig. 1B, D, F), while IL-10 increased only in TRLF + Rest animals proximally (Fig. 1H).

MicroCT Showed No Loss of Radial Trabecular Bone Volume, But Increased Anisotropy and Plate Like Structure

Morphological features of trabeculae in the radial metaphyses, analyzed by microCT, did not show significant changes across the groups in bone volume density (BV/TV), BS/BV, BS/TV, trabecular number, thickness or separation (Tb.N., Tb.Th. or Tb.Sp.; Fig. 2A–F). However, trabecular architecture changes were noticeable in 3D reconstructed images (Fig. 2G–I). Therefore, we examined the degree of anisotropy (DA) and structural model index (SMI). We observed that training and task performance lead to uneven trabeculae redistribution (i.e., increased DA), making the trabeculae

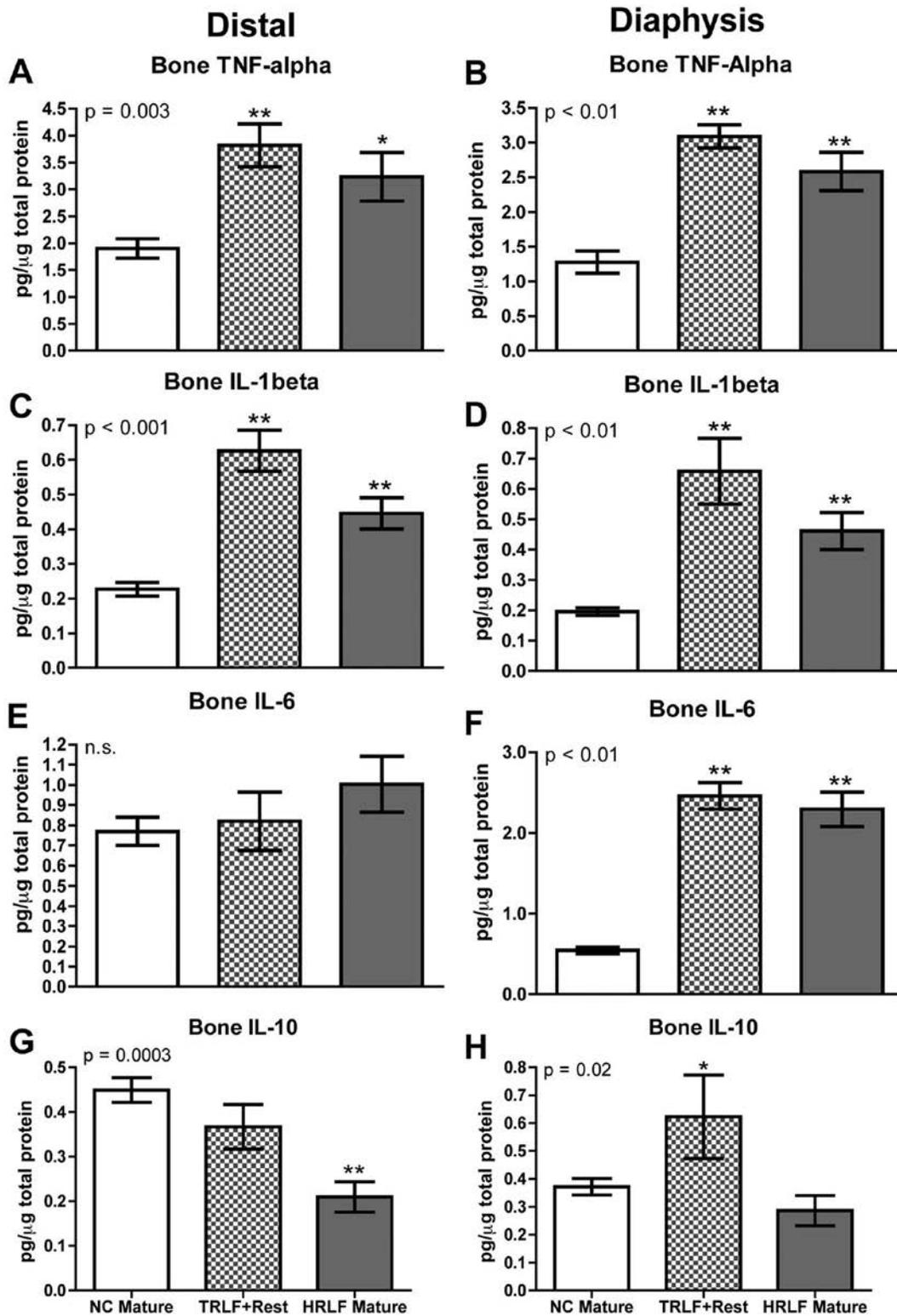


Figure 1. Bone cytokines, assayed using ELISA. After homogenization, forelimb bone supernatant was analyzed separately for the distal (radial and ulnar metaphysis, epiphysis and carpal bones) and proximal diaphysis (radial and ulnar diaphysis) regions in NC Mature, TRLF + Rest and HRLF Mature rats. **A-B)** TNF-Alpha levels in distal and diaphyseal bone. **C-D)** IL-1 beta levels in distal and diaphyseal bone. **E-F)** IL-6 levels in distal and diaphyseal bone. **G-H)** IL-10 levels in distal and diaphyseal bone. ANOVA p-values are reported on individual graphs.

* and **p < 0.05 and p < 0.01, compared to NC Mature rats.

Radius Trabeculae

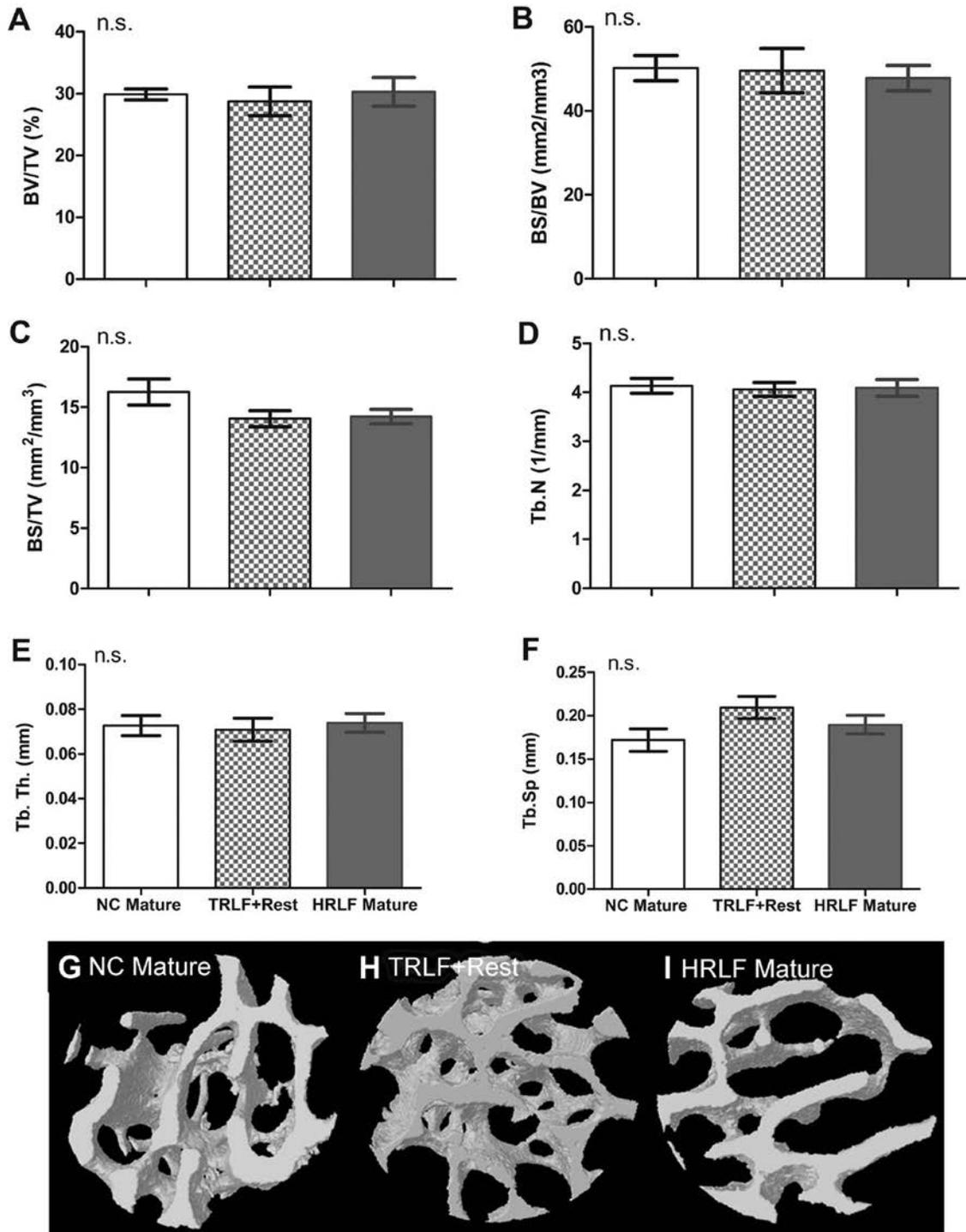


Figure 2. Micro-computed tomography (microCT) analysis of trabeculae in the distal radial metaphysis. **A)** Bone volume over tissue volume (BV/TV), **B)** bone surface over bone volume (BS/BV), **C)** bone surface over tissue volume (BS/TV), **D)** trabecular number (Tb.N.), **E)** trabecular thickness (Tb.Th.) and **F)** trabecular separation (Tb.Sp.) did not significantly vary in TRLF + Rest or HRLF Mature rats, compared to NC Mature rats. **G-I)** Reconstructed three-dimensional (3D) microCT transaxial images of the ROI of trabeculae in the distal radial metaphysis. n.s. = ANOVA was not significantly different.

Trabeculae Structure

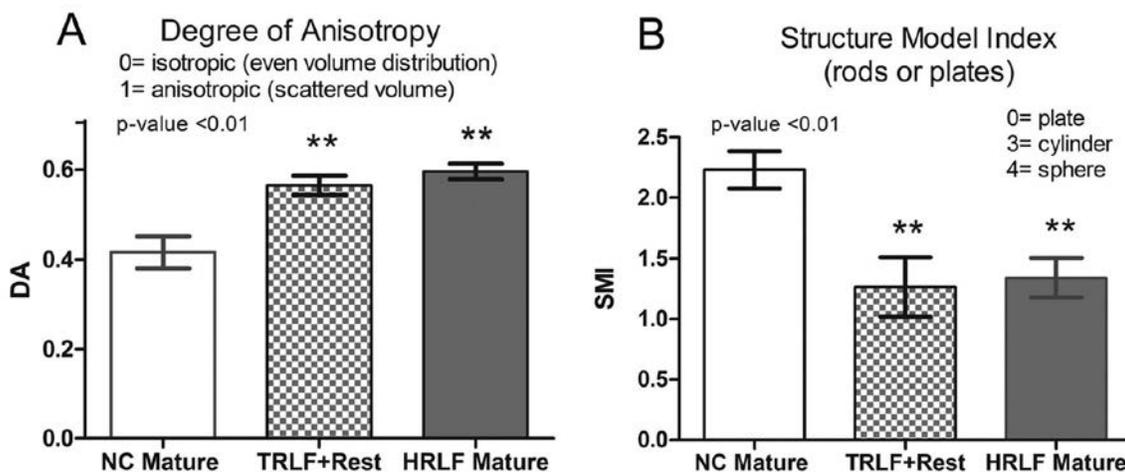


Figure 3. Trabecular microstructure analysis. **A)** Degree of anisotropy (DA) shows an increase with TRLF + Rest and HRLF12W Mature in disorganization of the trabeculae volume. Zero (0) is more isotropic (even distribution of volume) and one is indicative of anisotropy (scattered distribution). **B)** Structure model index indicates a slight increase towards the beneficial plate-shape with TRLF + Rest and HRLF task. ANOVA p-values are reported on individual graphs.

**p < 0.01, compared to NC Mature rats.

more scattered (Fig. 3A). Training and task performance also lead to conversion of a rod-like trabeculae structure, seen in NC Mature, to a more plate-like configuration in TRLF + Rest and HRLF Mature rats (Fig. 3B).

MicroCT Showed Loss of Radial Cortical Bone Quality

Interestingly, the radial diaphysis showed significant of cortical bone remodeling and degradation. The total cortical area (Ct.Ar., Fig. 4C) and total area (Tt.Ar., Fig. 4B) remained unchanged. In contrast, the marrow area (Ma.Ar.) was increased in TRLF + Rest and HRLF Mature animals (Fig. 4D), leading to a reduction in cortical thickness (Fig. 5E). More detrimental changes were observed as increased total porosity volume (Po.V., Fig. 4F), percentage of cortical porosity (Ct.Po., Fig. 4G) and pore density (Po.Dn., Fig. 4H) in TRLF + Rest and HRLF Mature rats, compared to NC Mature rats. Representative 3D images showing the visual differences are shown for NC Mature (Fig. 4I), TRLF + Rest (Fig. 4J) and HRLF Mature (Fig. 4K).

Discussion

We observed that inflammatory cytokines increased in distal and diaphyseal regions of TRLF + Rest and HRLF Mature bones, compared to NC mature rats, while a key anti-inflammatory cytokine decreased in the HRF + Mature rats. Micro-computed tomography analysis of TRLF + Rest and HRLF Mature bones showed that despite the increase in pro-inflammatory cytokines, that there was no significant loss in trabecular bone volume in the distal metaphysis of the radius. However, there were significant anisotropic and structure model index changes in the distal trabeculae. The mid-

cortical diaphyses of these same groups also showed endosteal resorption, cortical thinning and increased porosity, indicative of reduced cortical bone quality, compared to NC Mature rats. Thus, repetitive reaching and grasping at constant moderate loading levels, leads to increased bone inflammatory cytokines, reduced trabecular bone quality without loss of bone volume, and decreased cortical bone quality. Both of the latter bone changes are associated with increased fracture risk.

We have recently shown using ELISA that both the training period and performance of this same HRLF task for 12 weeks by young adult rats lead to no significant increases in pro-inflammatory cytokines in the distal forelimb bones,⁹ which is in contrast to the increases in IL-1beta, TNF-alpha and IL-6 observed in the mature trained and HRLF task rats in this study. The young adult rats used in that past study were 2.5 months of age at onset of the training, while the mature rats used in this study were 15 months of age. These findings of increased inflammatory cytokine production in mature rat tissues are consistent with our past findings of increased inflammatory cytokine production in serum and tendons of mature rats performing a HRLF task,^{12, 13} compared to young adult rats performing the same task. These serum changes were concomitant with enhanced task-induced degenerative changes in forelimb tendons in aged HRLF rats.¹² These results are consistent with other studies showing that aging mammals typically have increases in the same cytokines (IL-1beta, TNF-alpha and IL-6), in tissues and systemically, compared to young adult mammals, even in the absence of detectable tissue injury.^{14, 15} These cytokines are known to stimulate bone resorbing osteoclast formation and impair bone forming osteoblast differentiation,

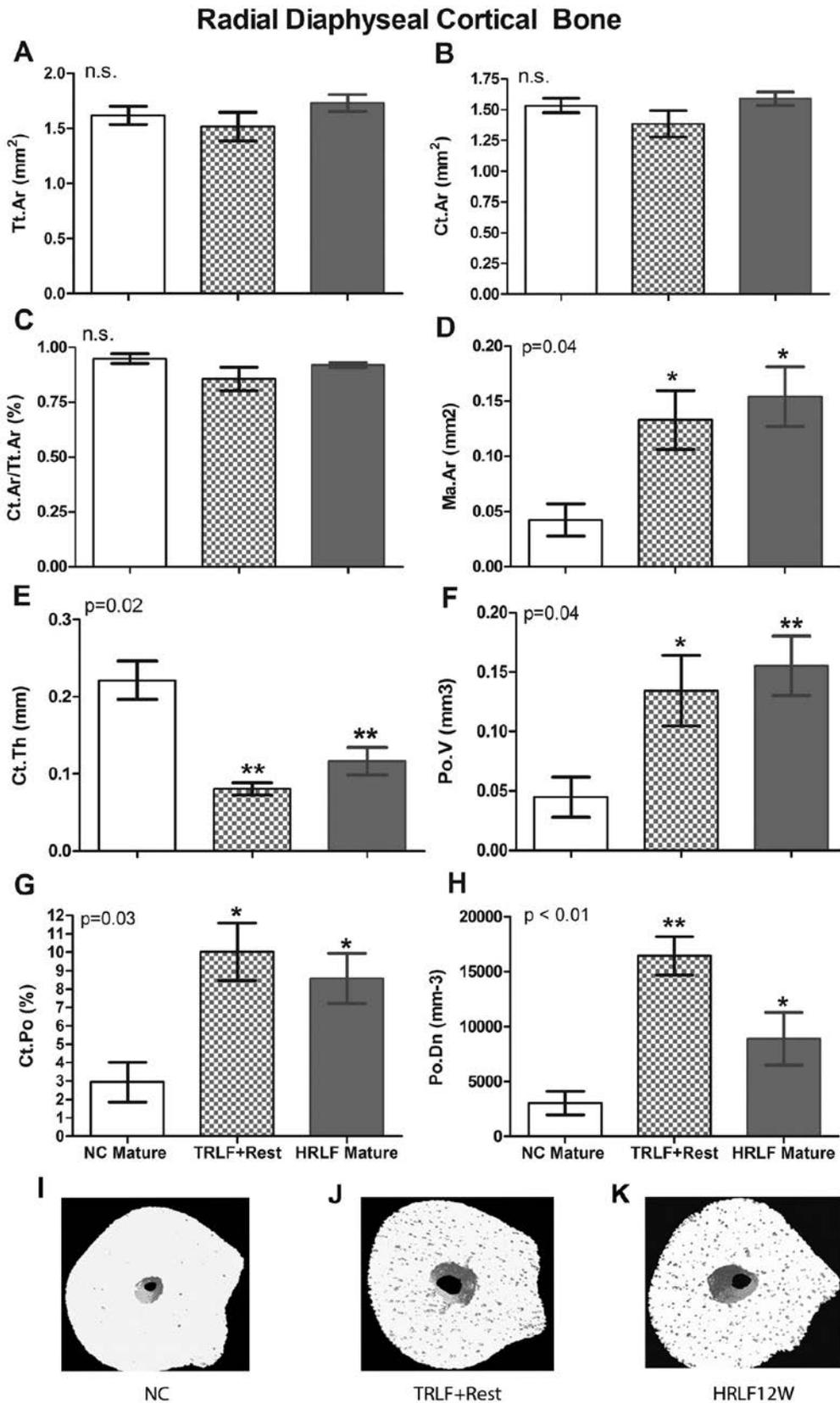


Figure 4. MicroCT diaphyseal cortical differences. (A) Total cross-sectional area inside the periosteal envelope (Tt.Ar), (B) cortical bone area (Ct.Ar), (C) cortical area fraction (Ct.Ar/Tt.Ar), (D) marrow area (Ma.Ar), (E) average cortical thickness (Ct.Th), (F) pore volume (Po.V), (G) percent cortical porosity (Ct.Po), and (H) pore density volume (Po.Dn). (I-K) Transaxial views of selected diaphyseal cortical volumes of interest. ANOVA p-values are reported on individual graphs. * and **p < 0.05 and p < 0.01, compared to NC Mature rats. n.s. = ANOVA was not significantly different.

which could lead to a net bone loss.^{16–20} Thus, the increase in cytokines in Trained + Rest and HFLF Mature rat forelimb bones could be contributing to the reduced quality in these bones.

Aging is associated with decreased bone quality and mass.^{8, 21–25} Although we did not see a reduction in bone volume in distal trabecular region of the radius, we observed altered trabecular structure (increased degree of anisotropy and a decrease in the structural model index), cortical thinning and increased porosity in the TRLF + Rest mature and HRLF Mature rats. The degree of anisotropy (DA) in trabecular bone is one of the most important determinants of mechanical bone strength;^{32, 33} its increase in the radius is suggestive of a decrease in strength in this region. We also observed a decrease in the structural model index (SMI) in the distal radial trabeculae. SMI is an architectural description of the rods versus plate shape of the trabeculae in 3D. Osteoporotic bone is characterized by a change from plate-like trabeculae to rod-like trabeculae.³⁴ The cortical thinning was due to endosteal resorption that was not matched by periosteal apposition after training and task performance. More detrimental changes were obvious as increased bone porosity, which is indicative of active Halverson system remodeling²² or increased resorption spaces,^{35, 36} changes implicated in skeletal fragility and stress fractures.^{8, 37} These results differ dramatically from our previous results in young adult rats, in which performance of the same HRLF task for 12 weeks induced anabolic changes in the distal trabecular region of the radius, including increased bone volume and increased trabecular thickness.⁹ Thus, we observed several changes in bone structure and quality in these mature rats that are also linked to increased fracture risk and perhaps even osteoporosis.

In conclusion, the combination of aging with prolonged performance of occupational repetitive tasks lead to decreased bone quality that has been associated with increased risk of fractures.

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Conflict of Interest: Current Concepts and the Recommendations for the Practicing Physicians

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Introduction

Awareness and understanding of what constitutes a conflict of interest (COI) in healthcare is vital to ensure proper patient care, uphold the high ethical standards of the profession, and to comply with regulatory statutes. The recent implementation of the Patient Portability and Accountable Care Act (PPACA or ACA),¹ and specifically the “Sunshine” provision contained therein constitutes a major effort at the federal level to increase transparency for transfers of value from pharmaceutical, device, and medical supply companies to physicians. Under this act, all gifts to physicians of a \$10.00 value or more will be posted on a public website. This has increased the scrutiny of physician benefits and sources of income.² Another federal statute, the Stark Law prohibits physicians from directing health care referrals or “business” to any entity in which they hold a financial interest or from which they receive something of value. Violations of the Federal Anti-Kickback and Stark Laws may result in substantial monetary penalties, exclusion from participation in health care programs, and imprisonment.³ In the current climate of increased regulatory burden resulting in increased administrative expense and declining reimbursement, the transition from a fee-for-service to a value-based model has caused the physician to experience a virtual or real decline in income. As such, secondary issues, such as financial gain⁴ may become a more central concern to the health care provider. This, in turn, may result in an unconscious, instinctive, psychological motivation for the physician to engage in relationships or transactions that constitute a COI.⁵ It is therefore imperative that physicians, particularly physicians in training, understand and recognize these concepts proactively.⁶⁻⁹

In this brief review, the relevant behavioral data will be examined, the necessity and purpose of disclosure discussed, and the pertinent legislation summarized.

Behavior

A COI in medicine exists when physicians’ secondary interests influence their decision-making in patient care, administrative issues or scientific research. Specifically, the influence from relationships between physicians and industry are of importance because they elicit two kinds of behavior: the tendency to default to one’s own self-interest and

the need to reciprocate.⁵ Both have strong subconscious foundations.

Self-interest refers to anything that could be considered desirable to the physician, such as monetary benefit or praise from peers. Its impact on physician decision-making may not be intuitively obvious. The literature is, however, clear. One study showed that when faced with two fairly equal choices, individuals will choose the one that is even slightly more self-beneficial; this effect can potentially subvert consciousness.^{10,11} In another study, Roth and Murnighan (1982) showed that people conflate their own interests with what is ethical. They designed an experiment where two subjects bargained over the distribution of 100 lottery tickets. A winning ticket paid \$20 to one subject and \$5 to the other. The results showed that the \$5 earners advocated for an equal monetary split and the \$20 earners advocated for an equal ticket number split,¹² suggesting an inability to consider the opposing view. Additionally, self-entitlement appears to positively correlate with personal struggles. Sah et al. (2010) showed that physicians reminded of personal sacrifices such as long work hours and incurred debt were more likely to condone the acceptance of gifts as compared with others who were not reminded.¹³

When individuals have unconscious desires or motivations for situational outcomes where they stand to benefit, they may rationalize their views by selective interpretation and explanation.¹⁴ Ditto and Lopez (1992) showed that people tend to look hardest for what they want to see. They conducted an experiment where subjects were told they were being tested for a dangerous enzyme deficiency. The subjects provided a saliva sample that was placed on a placebo test strip. Some were told if the strip turned green, they had the deficiency, while others were told if it turned green, they did not. Those subjects hoping for the strip to turn green waited much longer than those who hoped it did not.¹⁵ For physicians, this might mean justifying a COI based only on criteria that the physician wants to see — i.e., criteria that dismiss it as an actual COI. There may also be a tendency to ignore facts that support the opposing viewpoint. An experiment by Karlsson et al. (2006) showed people tend to look up the value of their stocks less often when the market is down than when it was up,¹⁶ suggesting they were less interested in bad news than good.

The desire to maintain an honest self-image and avoid a negative one¹⁴ does somewhat limit the degree to which individuals accept COI. In an experiment by Mazar et al. (2006) that evaluated whether decreasing the probability of being caught cheating affected the magnitude of deception, it was shown that individuals allowed themselves to cheat a little, but no more, suggesting they either feared being caught or felt guilty about what they did, or both.¹⁷ This suggests physicians might be more likely to engage in CsOI they can justify or that will not raise suspicion, such as accepting pens or pencils from a drug company representative, as opposed to an all-inclusive paid vacation.

Physicians might also be more likely to engage in CsOI if there are degrees of freedom between relationship and reward, as in the case of accrued credits that can be redeemed for a gift at a later date. As a follow up to their study in 2006, Mazar et al. (2007) showed the amount of cheating doubled when subjects received tokens for correct answers that could be exchanged for money, rather than money directly. The effect was attributed to the subconscious perception that the personal sense of guilt subjects experiences was reduced by being less-directly rewarded.¹⁸

Similar to self-interest, *reciprocity* has deep-seated evolutionary roots that can predictably influence the way a physician behaves. Such effects are measurable through Functional Magnetic Resonance Imaging (fMRI), which correlates the degree of blood flow in specific regions of the brain with decision making. King-Cases et al. (2005) looked at the relationship between behavior and trust through fMRI. "Investor" subjects decided how much money they would give to "trustee" subjects, and trustee subjects then determined how much they would return. Brain fMRIs were obtained periodically over many rounds. The researchers found activity in the head of the caudate nucleus correlated with whether trustees were going to increase or decrease repayment to investors, where the amount repaid represented the magnitude of trust between the parties. In early rounds, signal intensity correlated with the trustees' reactions to the immediate amount invested, but in later rounds correlated with its anticipation.¹⁹ The study suggests that the need to reciprocate, e.g., a tendency to prescribe a specific drug or use a specific device, is based on the degree of trust in a relationship, which in many cases reflects the "friendship" between physicians and industry representatives. This friendship, however, is not always genuine, and despite the best intentions, drug and device companies know that "friendship sells":^{5,22} pharmaceutical companies spend \$12 billion to \$18 billion annually marketing to physicians,²¹ much of this through direct face-to-face contact with industry representatives.

Another important mechanism that makes physicians susceptible to COI is the belief that they will not be swayed by biased information. This is certainly a factor in explaining why physicians will frequently meet with industry represen-

tatives despite an awareness of the potential COI implications. Chimonas et al. (2007) demonstrated this effect and showed a positive correlation between drug company-physician interaction and prescribing behavior of a marketed drug.^{23,24} Such effects were also found to be present in medical students.¹⁴

Disclosure

Disclosure is important in the management of COI, as it empowers the patient or reader to be the final arbiter of whether or not a conflict may exist. While disclosing a COI may appear to give an unbiased interpretative context to a physician's advice, two effects — strategic exaggeration and moral licensing — can often result in the opposite effect.^{10,26} *Strategic exaggeration* is the tendency to impart more biased information in order to offset what is being disclosed, essentially nullifying the intent of the disclosure. An example might include a physician disclosing his financial benefit to a patient he is trying to recruit for a clinical trial and then following the disclosure with information about how beneficial the new treatment has been. This, in effect, distracts the patient from considering the physician's advice in the context of his COI and may even deter the patient from seeking a second opinion.¹⁴

Moral licensing is the unconscious judgment that biased advice is acceptable because COI has been disclosed. It provides physicians with a false sense of security to impart advice regardless of how biased it may be.²⁶ Loewenstein et al. (2005) demonstrated the effect by designing an experiment where advisers would make recommendations to estimators to help determine how many coins were contained in a jar. The advisers were permitted to observe these jars close up and for extended periods of time, whereas the estimator could only observe for a short time and from a distance. Both the estimators and advisers were compensated based on the accuracy of their estimates, but the advisers were additionally compensated based on how high the estimates were. The results showed the advisers tended to overestimate the amount when their competing interests were disclosed, likely in an effort to compensate for lack of trust.²⁷

This does not nullify the importance of disclosure, since CsOI are ubiquitous in medicine and disclosure still remains the most feasible common pathway for an individual to determine credibility on their own. It suggests, however, that the advisee must be knowledgeable on how to detect bias and discount it if disclosure is to be effective.²⁸ Forced disclosure may deter involvement with avoidable CsOI because of reputational concerns. For example, accepting a calendar from a pharmaceutical company is not likely to alter public perception about a physician's ethical choices, but accepting an invitation to a weekend golf retreat might. Physicians may therefore be more apt to engage in CsOI that on the surface appear benign but are CsOI nonetheless.^{28, 29, 30}

The Current Environment

The physician-hospital relationship is changing dramatically. With the number of doctors employed by hospitals increasing in recent years (32%, from 2000 to 2010³¹), physicians must understand aims or goals of the hospital may not be identical to theirs. Specifically, two policies merit scrutiny: COI credentialing and economic loyalty policies. Both represent efforts by hospitals to avoid competition and protect their interest by leveraging the financial position of physicians.

COI credentialing is a form of exclusivity: physicians are forbidden to seek medical staff appointments at other hospitals or to admit patients at unaffiliated health care facilities. Economic loyalty policies limit the ability of physicians to participate in activities that compete against the economic interests of the hospital. Both are effective because many physicians depend on treating hospitalized patients and having access to managed care provider panels for income. Consequently, they cannot afford to jeopardize their source of income by failing to comply with a COI credential policy.³² While both practices are not explicitly illegal, they affect patient health care by limiting access. In a given community, physicians are prohibited from developing or participating in a competing facility that could possibly offer greater benefit to the patient. Insurance plans also limit where a patient can seek treatment because reimbursement is frequently dependent on physician referrals, and physicians are only able to refer within their hospital network.³²

As governmental funding sources have declined, the influence of the industry has increased. Physicians represent a large target market, as 80% of all health care expenditures depend on their advice and recommendations to patients.³³ Understanding these mechanisms can help physicians consider the impact they may have on patient care.

Industry utilizes two broad strategies to promote their products: push and pull. *Push strategies* rely on marketing products to physicians with the hope that they are utilized for patient care. The marketing occurs in the form of gifting promotional items such as pens, pencils, mugs, and calendars, all of which include the company name or logo, favors, meals or any initiative that directly or indirectly benefits the physician.³⁴ While the Pharmaceutical Research and Manufacturers of America³⁵ have discouraged such gifts unless they have educational purpose and do not exceed \$100 in value, compliance is voluntary.^{36,37} For those in compliance, representatives will often provide “reminder” items at carefully selected time intervals, which include anatomic models, stethoscopes, and textbooks.³⁸ It costs five to 10 times as much to gain a new customer-physician than it does to retain an established one;³⁹ hence, persistence pays.

Pull strategies rely on advertising and sales promotion to patients. Companies then expect patients to bring the product to the attention their physician. Direct-to-consumer marketing has become increasing popular over the last few

decades, with industry spending approximately \$40 million in 1989, \$350 million in 1995,⁴⁰ and \$2.3 billion in 2000.⁴¹ The trend reflects its effectiveness. In a study by Huang et al. (2000), 33% of those who saw an advertisement for a specific pharmaceutical product asked their physician for that product. Of those, 75% were prescribed the drug requested.⁴² This appears consistent with the finding by Paul et al. (2002), which showed 63% of primary care physicians felt pressured to prescribe drugs that patients brought up.⁴³

Taken in the context of the behavioral data noted above, and the increased regulatory burden to be discussed below, it is clear that a prudent and transparent relationship with industry is the order of the day. While industry is a valuable partner in patient care, education and research, neither the practitioner nor the scientist must realize that the ultimate goals of industry and medicine are divergent. As noted above, disclosure is a major step in transparency and appropriate management of real or perceived COI; federal legislation codifies and requires it.

Relevant Legislation

Historically, government regulation has targeted manufacturers regarding inappropriate relationships with physicians. The physician is now the subject of similar regulation.⁴⁴ The increased monitoring and public disclosure of payments from companies to physicians has made targeting physicians easier;⁴⁶ aside from ethical considerations, it is, thus, important from a practical and legal standpoint that physicians understand what constitutes *legally reprehensible behavior*. Four major articles of legislation are directly relevant: the Stark Law, the Sunshine Act, the Anti-Kickback Statute, and the False Claims Act.

The Stark Law (Figure 1) is intended to govern physician self-referral of Medicaid and Medicare patients. It prohibits a physician from referring those patients to any entity with which the physician, or a member of the physician’s immediate family, has a financial relationship. For the Stark Law to apply, the referral must be for designated health services (DHS, for a complete list: http://www.cms.gov/physicianreferral/40_list_of_codes.asp) reimbursed by Medicare, and the receiving party must meet the defining “entity” criteria.⁴⁷ The law was written under the premise that physician self-referral constitutes an inherent conflict of interest which excessively increases the use of health care services.^{48, 49, 50-52, 53}

Under Stark, an entity is a solo or group practice, corporation or partnership that renders DHS services. It may or may not bill Medicare directly for those services.⁵⁴ Immediate family members include husband, wife, mother, father, sibling, or child, stepparent, stepsibling, or stepchild, father-in-law, mother-in-law, brother-in-law, sister-in-law, grandparent or grandchild, spouse of a grandparent or grandchild.

Two categories of prohibited financial relationships exist: those associated with ownership and investment interests and those associated with compensation arrangements. Each

may be either a direct or indirect relationship.⁵⁵ Ownership and investment interests include equity, debt, stock, loans, and bonds.⁵⁶ Compensation arrangements involve money.⁵⁷ Indirect relationships link a physician with an entity through at least one intermediary, whereas direct relationships do not.⁵⁸ A direct interest, for example, could involve a physician holding partial stock in a physical therapy practice to which he/she refers. If the stepson of a physician owns a nursing home and the nursing home owns partial stock in the physical therapy practice, the physician would be considered to have a vested interest in the profitability of the physical therapy practice as well;⁴⁹ this is an indirect interest.

Penalties for violation of the Stark Law are significant, and they may include denial or refund of payment for services rendered as a consequence of the improper referral, exclusion from federal health care programs, and civil monetary penalties. Civil monetary penalties are substantially higher (up to \$100,000 vs. \$15,000) if the physician knowingly engages a circumvention scheme or cross-referral arrangement. For example, consider a scenario where Physician A and Physician B have ownership interests in Treatment Facility A and B, respectively. Both physicians cannot refer patients to their respective treatment center because it constitutes an obvious COI, but they also cannot refer patients to the other physician's treatment facility if a referral agreement exists. Such an agreement would involve Physician A sending all his patients to Treatment Facility B and Physician B sending all his patients to Treatment Facility A.^{49, 59-62}

The Sunshine Act is a provision of the *Patient Protection and Affordable Care Act (PPACA)* that is intended to increase the transparency of physician-industry relationships by requiring pharmaceutical, device, biological, and medical supply companies to disclose payments and other transfers of value associated with products covered by Medicare, Medicaid, or Children Health Insurance Program (CHIP) to physicians and teaching hospitals.¹ The act also requires companies to disclose ownership and investment interests held by physicians or their immediate family members.⁶³ The information will be available online and searchable by manufacturer, physician, and teaching hospital name.² All of the following are considered payments and will be posted: cash or a cash equivalent, items or provided services, stock, stock options, or any other ownership interest, dividend, profit, or return on investment, consulting fees or compensation for services, honoraria, and gifts, or charitable contributions, food, entertainment, or travel, education or research, including grants and compensation for speaking at medical education programs, current or prospective ownership or investment interest.⁶⁴

Payments are reported annually to the Centers for Medicare and Medicaid Services (CMS), a federal agency with the United States Department of Health and Human Services (HHS).⁶⁵ Manufacturers and Group Purchasing Organizations (GPOs) issuing payment are responsible for reporting; recipient physicians are not. Among other criteria, the reports

will include:⁶⁶ the name of the manufacturer or GPO issuing payment, the recipient physician's name, specialty, business street address, and national provider identifier (NPI), the amount, date, form, and nature of the payment, the name of the associated covered drug, device, biological, or medical supply, and whether or not the payment was to a physician holding ownership or investment in the applicable manufacturer. Payments and transfers of value do not have to be reported if they meet any of the following criteria:^{64, 67} are individually less than \$10 and do not aggregate above \$100, consist of educational materials that direct benefit patients or are intended for patient use, and are received from a third party where the manufacturer is unaware of the physician's identity

The disclosure of payment does *not* indicate or imply the presence of a conflict of interest. Its presence on the CMS website merely serves the purpose of providing objective information on the types of relationships between manufacturers and group purchasing organizations (GPOs), and physicians. However, this does not preclude its use in prosecuting physicians for violations of the Anti-Kickback Statute, False Claims Act (FCA), or Stark Law. The website will also contain information about enforcement action taken the previous year.^{2, 68, 69}

It is thus imperative that physicians monitor this information for accuracy. Physicians registered on the CMS website are notified by CMS 45 days prior to public disclosure and can contest inaccurate information during this time. If a dispute arises, a 15-day resolution period is granted that allows the manufacturer or GPO to correct the information. The information may be repeatedly contested if it is not correct. Data that becomes publically available but still remains contested is marked as "disputed."⁷⁰

The Anti-Kickback Statute (Figure 1) is a criminal statute that forbids a physician from knowingly receiving remuneration in exchange for referrals and services.⁷¹ The statute necessitates intent. Per the Office of the Inspector General (OIG), intent is met if a purpose of remuneration is to induce referrals for, or purchases of, an item or service covered under a federal health program. The amount of remuneration is irrelevant,⁷² as are any additional good intentions that may exist with regard to such an arrangement.⁷³

Fee-splitting is also illegal under this statute. Fee-splitting is considered to be means by which physicians increase profits by charging clients substantially more for tests that they themselves pay less for. Consider the example whereby a physician contracts with a local pathology lab to read slides. The physician pays a volume based a discounted price to the lab and does not pass such discounts on to the patient and charges a substantially increased price. This constitutes fee-splitting and sets a precedent for not only overbilling federal health care programs but for potentially exposing the patient to unnecessary tests at the expense of increased profits.⁷⁴

Violations of the Anti-Kickback statute can result in both criminal and civil penalties, up to \$25,000 in fines and five

Figure 1. How Does the Anti-Kickback Statute Differ from the Stark Law⁸²?

- **Prohibition:** The Anti-Kickback Statute prohibits offering, paying, soliciting, or receiving *anything* of value to induce or reward referrals, whereas the Stark Law prohibits a physician from referring Medicare patients for *designated health services* to an entity with which the physician has a financial relationship.
- **Referrals:** The Anti-Kickback Statute includes referrals from anyone, whereas the Stark Law includes referrals only from a physician.
- **Intent:** Intent must be proven under the Anti-Kickback Statute, whereas no intent standard for overpayment is necessary under the Stark Law. However, intent is required for civil monetary penalties for knowing violations under the Stark Law.
- **Penalties:** Violations of the Anti-Kickback Statute may result in criminal penalties, which include fines up to \$25,000 per violation and up to a five-year prison term per violation, or civil penalties, which include up to \$50,000 per violation. Violations of the Stark Law only result in civil penalties, which may include overpayment/refund obligations and up to \$15,000 per violation. Both laws may also civilly result in False Claim Act liability, program exclusion for violations, and civil assessments of up to three times the amount claimed/received.
- **Exceptions:** Meeting requirements for exceptions under the Anti-Kickback Statute are voluntary, whereas meeting requirements for exceptions under the Stark Law are mandatory. In other words, if an arrangement does not comply with a safe harbor, it may not necessarily violate the Anti-Kickback Statute, but if an arrangement does not comply with a Stark Law exception, it constitutes a violation.
- **Federal Health Care Programs:** The Anti-Kickback Statute applies to all federal health care programs, whereas the Stark Law applies only to Medicare and Medicaid.

years in prison per violation, and from Medicare and Medicaid participation and fines up to \$50,000 per violation plus triple the amount in question, respectively.⁷²

Physicians are, however, protected from prosecution under the Anti-Kickback statute if their activities or arrangements are considered “safe harbors.” Safe harbors were exceptions instituted by congress in response to the potential breadth of improper application of the Anti-Kickback Statute.⁷⁵ Of particular importance are those that deal with investment interests, referral services, and discounts.

Investment interests are protected providing the physician is not individually receiving remuneration in exchange for referrals to an unfair degree. This is particularly relevant for a financial interest in hospitals and departments. A physician is permitted to have a stake in an entire hospital because financial benefit from referrals to that hospital is considered insignificant. The COI is not considered insignificant if the physician has complete ownership of a subdivision or department because of internal referrals, thereby benefiting individually and completely.⁷²

Physician investment is also permitted to invest in an ambulatory surgery center (ASC) providing that he/she owns no more than 40% of the ASC, and completely discloses the ownership interest to patients. This is permitted due to the rationale that ASCs can often deliver services at lower costs than hospitals for similar procedures.^{77, 78} However, physicians are urged to utilize caution. It has been shown that physicians are more likely to refer well-insured patients to these facilities than they are Medicaid patients, which reimburse less, a clear COI. Additionally, physicians are still

prohibited from referring patients to facilities that they own in numerous other categories.⁷⁹

Referral services include professional societies and other consumer-oriented groups that refer patients. Physicians who pay fees to these organizations to be listed on their referral lists are protected providing the fees only reflect operational costs. Fees cannot be based on the volume or value of any referrals.^{79, 80} Cross-referrals, however, are permissible. A cross-referral permits one physician to refer a patient to another physician, who later refers the patient back to the original referring physician. This safe harbor exists to permit what otherwise constitutes a normal everyday referral. No payment, however, is permitted for the re-referral.^{79, 80, 81}

The False Claims Act (FCA) is a statute that protects the federal government from being overcharged.⁸³ It imposes liability on any person who submits a claim to the federal government that they know (or should know) is false. The law also forbids the creation or use of false records in order to justify payment from the federal government.⁸⁴ “Should know” means that the physician does not have to have actual knowledge that the claim is false. If he acts in reckless disregard or in deliberate ignorance of the truth, he is liable.^{84, 85}

Violations of the FCA may result in fines of \$5,500 to \$11,000 per claim, plus three times the government’s damages.⁸⁵ Most physicians generate a bill for each set of services rendered per patient. While the billed amount may be relatively inexpensive, many thousands of bills are usually submitted per year. Each bill is susceptible to its own fine. In comparison, treble damages represent a relatively small component.⁸⁴

Public and internal monitoring has been encouraged and rewarded by *qui tam*. A *qui tam* action allows private persons to file suit for violations of the FCA on behalf of the federal government. They are entitled to a percentage of the amount recovered by the federal government. A private person includes anyone aware of the illegal claiming actions, such as office and billing staff. The *qui tam* creates a precedent these individuals to come forward by rewarding them.⁸⁴

Conclusions and Suggestions

The climate in which healthcare is delivered is changing rapidly. Increased regulation, declining reimbursement, public and governmental suspicion have resulted in increased critical scrutiny of medical science and practice. Only by understanding the substance and implications of COI, managing COI with robust disclosure and complying scrupulously with governmental regulation do we, as physicians, have a chance to serve our patients and profession properly. In an effort to do so, the authors suggest the following questions be considered as a beginning for self examination.

1) Are there professional issues that might be constituted as a conflict of interest?

Conflict of interest issues include professional and business interests of the physician as well as institutional and

organizational relationships that might alter or affect the clinical treatment of patients. As discussed previously, such conflicts can subconsciously affect the physician's ability to make an unbiased decision, even if the physician feels it plays no role. For clear CsOI, the recommendation is divestiture or termination of the contract or relationship in question.

2) Are there legal, public health, or safety consequences that might affect clinical decision making?

Legal rules may, effectively, impose limits on the ethical options of physicians, as in the case of violating physician-patient confidentiality or the prescription of regulated medication. Public health and safety concerns may also necessitate breaches in confidentiality and as well as preventative measures to ensure public well being. If such dilemmas occur, consultation with a regulatory expert or ethicist is recommended.

3) Are there parties other than clinicians and patients who have an interest in clinical decisions?

Other parties include the patient's family, hospital and managed care administrations, public health authorities, third-party payers, employers, police officers, lawyers etc. The legitimacy of such claims raises various ethical issues for the physician that may impede the delivery of care, and have clear legal ramifications. For these reasons, any professional or business relationship with a close relative, as defined above, should be approached with extreme caution.

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Senior Abstract



Senior Bio Questionnaire

- Full Name: Scott Ethan Barbash
- Birthdate: 9/29/1982
- Hometown: Old Tappan, NJ
- Undergraduate School: University of Pennsylvania
- Undergraduate Degree: Bachelor of Science in Economics, Bachelor of Applied Science in Biomedical Engineering
- Medical School: Albert Einstein College of Medicine
- Fellowship: Sports Medicine – University of Virginia
- Significant Other: Tamar
- Children: Matthew
- Hobbies: Skiing, being a sports fan, enjoying time with my family
- Favorite Sports Team: New York Giants, New York Mets, New York Knicks
- Desired Practice Location: New York or Philadelphia
- Catch Phrase/Motto/Favorite Expression/Advice: “Punch the keys!”, “Implant, comin’ in hot!”

Optimal Differentiation of Tissue Types Using Combined Mid and Near Infrared Spectroscopy

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Introduction: Despite the number of anterior cruciate ligament reconstructions performed every year, the process of ligamentization, transformation of a tendon graft to a healthy functional ligament is poorly understood. Fourier transform infrared (FT-IR) spectroscopy is a technique sensitive to molecular structure and composition changes in tissues. FT-IR fiber optic probes combined with arthroscopy could prove to be an important tool where nondestructive tissue assessment is required, such as assessment of graft composition during the ligamentization process. The mid-IR spectral absorbances from connective tissues are well understood, but mid-IR radiation has limited penetration, through only ~10 microns of the tissue. In contrast, near infrared (NIR) has deeper penetration depth (mm to cm), but the spectral absorbances are much weaker and not as well understood. Combining these two spectral regions may provide valuable information about the sample composition. Previous studies in the food industry have shown that combining NIR and MIR spectroscopy resulted in optimal differentiation of composition. Mid-IR fiber optic probes have previously been used to differentiate between normal and pathologic connective tissues, and a recent study by our group has shown that the fiber optic probe spectral parameters correlate with cartilage histological grading. NIR fiber optic probes have been used during arthroscopy to evaluate the degree of degeneration of cartilage. The aim of this study was to combine and compare the use of MIR and NIR to differentiate regions within the ACL, and to differentiate ACL versus patellar tendon, as a preliminary study towards better understanding the ligamentization process *in vivo*. We hypothesize that the combination of NIR and MIR spectra will result in better differentiation compared to NIR or MIR spectroscopy alone.

Methods: Bovine ACLs (n = 3) and patellar tendons (n = 3) were dissected from freshly slaughtered 2–14 days old calves (Green Village, NJ). NIR spectra were collected in diffuse reflectance mode using a 3 mm diameter NIR fiber optic probe (Art Photonics, Berlin, Germany) coupled to a Matrix-F infrared spectrometer (Bruker, MA). Spectra were collected from two points at the midsubstance, the femoral and tibial insertion sites of each ACL and patellar tendon (4000 to 11,000 cm⁻¹ at 32 cm⁻¹ spectral resolution with 128 co-added scans). At each data point three spectra were collected thus resulted in a total of 72 spectra. MIR spectra were collected from the same location as NIR data using a Thermo Scientific Nicolet iS5 FT-IR spectrometer fitted with a fiber optic coupler (Harrick Scientific Products, Inc., Pleasantville, New York) and a silver halide attenuated total reflectance (ATR)-loop mid-infrared fiber optic probe (Art Photonics, Berlin, Germany) at 8 cm⁻¹ spectral resolution, with 32 co-added scans in the frequency range of 600-2000 cm⁻¹.

Data Processing: The spectra were processed using Unscrambler 10.1 (CAMO, NJ). The spectra were pretreated with a multiplicative scatter correction (MSC) followed by second derivative (savitzky golay, 3rd polynomial order, 11 point smoothing for MIR and 21 point smoothing for NIR data). A concatenated matrix was formed with NIR and MIR spectra where rows were comprised of NIR and MIR spectral absorbances from same sample as well as same location. MIR and NIR spectra were pretreated separately. Combined spectra were normalized by the standard deviation at each wavelength in the entire spectral collection. Separate partial least square discriminant analysis (PLS-DA) models with random cross validation were performed to differentiate ACL versus patellar tendon (11 segment with six samples) and insertion site versus midsubstance within the ACL (seven segments and four samples) using NIR spectra, MIR spectra and NIR and MIR combined together.

Results and Discussion: MIR spectra from ACL and patellar tendon were dominated by collagen peaks at 1650 (amide I), 1550 (amide II), 1338 (side chains) and 1240 cm⁻¹ (amide III) which result from vibrations of the peptide bonds (also present to lesser amounts in proteoglycans, (PG)), and by PG sugar ring vibrations, 985–1140 cm⁻¹. NIR spectra of ACL and patellar tendon were dominated by water peaks at 5200 cm⁻¹ and 6890 cm⁻¹. To discriminate ACL and tendon, the best PLS-DA classification was based on MIR spectra alone, which resulted in 97.2% accurate classification. However, to discriminate insertion sites and midsubstance regions within the ACL tissue, PLS-DA based on combined use of NIR and MIR resulted in the best classification (87.1%).

Discussion: The loadings (which reflect the spectral features that contribute to the model) for the MIR spectra PLS-DA model of ACL versus patellar tendon classification were dominated by the amide II absorbance at ~1550 cm⁻¹, likely reflecting differences in collagen and PG content in these two tissues at the surface. Ligament is a heterogeneous tissue, and its matrix composition varies throughout the length and depth. MIR alone did not perform well to classify different regions of ACL, likely due to the limited penetration of the MIR radiation which could not fully interrogate the ACL structure. However, addition of the NIR spectral region resulted in better discrimination between insertion sites and midsubstance within the ACL tissue. The loadings for PLS-DA model based on combined MIR and NIR spectral regions were dominated by water peaks at ~5200 cm⁻¹ and 7000 cm⁻¹, and by matrix peaks at 1079 cm⁻¹, 1250 cm⁻¹, 1643 cm⁻¹, 4300 cm⁻¹ and 4700 cm⁻¹. It should be noted that both spectral regions contributed towards differentiation of ACL regions, with the dominant frequencies arising from both water and matrix components.

Significance: The combination of NIR and MIR spectral regions could lead towards better understanding of healing of various orthopedic tissues, and effect of therapeutics and treatment modalities.

Senior Abstract



Senior Bio Questionnaire

- Full Name: Richard Jinwhan Han
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- Undergraduate School: Hillsborough, CA
- Undergraduate Degree: BA (Molecular and Cell Biology – Genetics)
- Medical School: Georgetown University
- Fellowship: University of California, San Francisco – Sports Medicine
- Significant Other: Aimee Reilly Han
- Children: Roxy (dog)
- Hobbies: Cooking, being a foodie, international travel, snowboarding
- Favorite Sports Team: San Francisco Giants
- Desired Practice Location: San Francisco, CA or Washington, DC
- Catch Phrase/Motto/Favorite Expression/Advice: YOLO

Vascular Complications in Total Knee Arthroplasty: A Newly Recognized Complication and Lessons from Our Practice

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Introduction

Vascular injuries are a rare but potentially devastating complication of total knee arthroplasty (TKA). We report our vascular injuries from a high volume community-based practice, including a previously unreported type of injury in the orthopaedic literature.

Methods

We retrospectively reviewed morbidity and mortality data and associated records at our institution over a 12-year period from 2001 through 2012. We included all primary TKAs performed by 10 orthopedic surgeons (three accounted for over 80% of cases). The majority of these TKAs were performed using a minimally invasive approach.

Results

Over this period, seven vascular injuries were identified out of 5,166 TKAs (0.14%); three acute vascular injuries (laceration/puncture, 0.06%), two popliteal thromboses (0.04%) and one popliteal pseudoaneurysm (0.02%). We also had a case of an arterial thromboembolic event secondary to discontinuation of anticoagulation in a patient with atrial fibrillation, a previously unreported event in orthopaedic literature. A minimally invasive approach was not associated with an increased risk of vascular complications. There were no amputations or mortalities due to these injuries in our group.

Conclusion

Vascular injury is a rare complication with a rate of 0.14% in our population. Although acute laceration/puncture was the most common injury seen in our patients, arterial thrombosis after discontinuation of anticoagulation is a potential complication of which the orthopaedic surgeon should also be aware. Early awareness and recognition is the key to avoiding long-term sequelae.

Senior Abstract



Senior Bio Questionnaire

- Full Name: Emeka James Nwodim
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- Undergraduate School: Temple University
- Undergraduate Degree: BA Chemistry, Political Science
- Medical School: Temple University School of Medicine
- Fellowship: University of Maryland Spine Program
- Significant Other: None
- Children: None
- Hobbies: Basketball
- Favorite Sports Teams: Baltimore Ravens/Philadelphia Eagles/Miama Heat
- Desired Practice Location: Undecided
- Catch Phrase/Motto/Favorite Expression/Advice: 1. Attitude of Faith, 2. Knowledge is useless unless converted to Wisdom, 3. "Hand Dominance?"

Effects of Shear Loading on Repaired and Unrepaired Longitudinal Vertical Meniscal Tears

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Introduction: Effects of shear loading on menisci on intact, *ex vivo* bovine knees is poorly understood. Many prior biomechanical studies have loaded excised, repaired menisci in tension and three studies have loaded excised menisci in shear. These studies hypothesized that shear force plays a more important role in stressing meniscal tear repairs. This study endeavored to describe the impact of shear loading on various commercially available meniscal repair systems on in situ menisci.

Methods: Four cm long longitudinal vertical tears were created in the posterior horn of the medial meniscus in 32 adult, fresh frozen, hind bovine knees. This group was subdivided into control (no repair), inside-out repair with a vertical mattress technique using No. 2 FiberWire, all-inside technique using No. 0 Orthocord with two PEEK anchors, and an all inside technique using No. 0 braided polyester suture with two flexible anchors (poly levo lactic acid or poly-acetal). The four groups of eight specimens were tested on an MTS Landmark 370.10 servo-hydraulic test system fitted with an Interface model 5200 multi axis load cell which enabled measurements of thrust and two separate moments. Each specimen underwent four rounds of 2,500 cycles at 2 Hz for a total of 10,000 cycles. In addition to data recorded by the multi-axis load cell, the cross-head displacement and total applied load were measured using machine transducers built in to the MTS. The machine design was capable of generating measurable shear loading on each sample. Primary outcomes measured between groups included stiffness, magnitude of shear stress, subsidence, amount of wear on repair device and amount of wear on menisci and the chondral surface. Statistical analysis was performed with JMP 8.0.1 software with two sided $p < 0.05$. An ANOVA test was used to compare the four study groups. A matched paired t-test was used to test for significant changes in mechanical characteristics between rounds of testing. A students t-test was used to compare the mechanical characteristics between groups of similarly scored repair devices and meniscal tissue samples.

Results: No statistically significant differences in geometric measurements (femoral length $p = 0.31$, tibial length $p = 0.41$, total length $p = 0.09$, flexion angle $p = 0.08$, max. valgus angle 0.75 , area $p = 0.2$), compressive stress ($p = 0.77, 0.63, 0.78, 0.86$ respectively), subsidence ($p = 0.57, 0.36, 0.36, 0.47$ respectively), stiffness ($p = 0.11, 0.43, 0.3, 0.22$), or calculated shear force ($p = 0.09, 0.09, 0.24, 0.62$) were found between the four study groups (unrepaired, No. 0 Braided polyester suture, No. 0 Orthocord, Vertical Mattress). In the vertical mattress group, two samples demonstrated minimal knot slippage and only one of those two showed some mild meniscal fraying around the repair. In the same group, another sample with no measurable repair device failure demonstrated mild meniscal fraying around the repair. In the Orthocord with two PEEK anchor group, two samples had some minimal knot slippage and two other specimens had some mild meniscal fraying around the repair. In the braided polyester suture with two flexible anchor group, three samples demonstrated minimal knot slippage and one other sample showed mild meniscal fraying. The unrepaired group had four samples with significant fraying and lengthening of the tear and four other samples had significant chondral wear on the articular surfaces. The unrepaired group demonstrated significant differences in the compressive stress between samples exhibiting significant meniscal fraying and also those exhibiting chondral wear ($p = 0.012, 0.005, 0.036, 0.004$) at each time point and significant difference in the magnitude of shear force at the same time points ($p = 0.035$).

Discussion: This is the first study to examine the effects of shear loading and fatigue on various repair techniques of vertical longitudinal meniscal tears in intact adult bovine knees. The study results support the efficacy of the machine design capable of simulating *in vivo* shear loading of menisci in intact bovine knees. The three repair groups demonstrated no statistically significant differences in any of the primary outcome measures. The statistically significant differences between repaired and unrepaired samples supports the importance of restoring normal anatomy after sustaining a meniscal tear.

Senior Abstract



Senior Bio Questionnaire

- Full Name: Samuel P. Popinchalk
- Birthdate: 12/19/1978
- Hometown: West Hartford, CT
- Undergraduate School: Worcester Polytechnic Institute
- Undergraduate Degree: BS Biotechnology
- Medical School: Tulane University School of Medicine
- Fellowship: Spine, University of Miami — Jackson Memorial Hospital
- Significant Other: Celine McGee — For all your support, my gratitude is immeasurable
- Children: None
- Hobbies: Golf, Reading
- Favorite Sports Team: New England Patriots
- Desired Practice Location: Philadelphia, PA
- Catch Phrase/Motto/Favorite Expression/Advice: Thoder's Five Fingers of life: 1. Work hard, play hard, 2. Don't ask someone to do something you won't, 3. Eat when you can, 4. Learn something new every day, 5. There are three sides to every story

Is Chemical Incompatibility Responsible for Chondrocyte Death Induced by Local Anesthetics?

M.T. BOGATCH, D.G. FERACHI, B. KYLE, S. POPINCHALK, M.H. HOWELL, D. GE, Z. YOU, F.H. SAVOIE

Temple University Hospital, Department of Orthopaedics, Philadelphia, PA

Background

Chondrolysis associated with intra-articular administration of local anesthetics has been attributed to chondrocyte death induced by the local anesthetics. The mechanism of how the local anesthetics cause chondrocyte death is not clear.

Purpose

This study was conducted to determine whether and how the local anesthetics cause chondrocyte death.

Methods

Bovine articular chondrocytes in suspension culture were treated for one hour with phosphate-buffered saline or phosphate-buffered saline/medium mixture (as controls); 1% lidocaine alone; 0.25% to 0.5% bupivacaine alone; phosphate-buffered saline with pH values of 4.5, 3.8, 3.4, and 2.4; or mixtures of the local anesthetics and cell culture medium or human synovial fluid. Chondrocyte viability was analyzed by flow cytometry using the LIVE/DEAD Viability/Cytotoxicity Kit.

Results

In 1% lidocaine-alone or 0.25% to 0.5% bupivacaine-alone groups, the rate of cell death was 11.8% to 13.3% of bovine articular chondrocytes, whereas the phosphate-buffered saline control had 8.4% of cell death. Increased chondrocyte death was only found when the pH value of phosphate-buffered saline dropped to ≤ 3.4 . In contrast, when bupivacaine was mixed with cell culture medium, needle-like crystals were formed, which was accompanied with 100% death of chondrocytes. Lidocaine did not form visible crystals when it was mixed with culture medium, but the mixtures caused death of over 96% of chondrocytes ($P < .001$).

Conclusion

Less than 5% of chondrocyte death was attributable to the anesthetics when applied to the cells alone or in phosphate-buffered saline-diluted solution. Acidity (as low as pH 3.8) or epinephrine in the anesthetic solutions could not account for chondrocyte death. However, chemical incompatibility between the local anesthetics and cell culture medium or human synovial fluid may be the cause of chondrocyte death.

Clinical Relevance

Intra-articular administration of lidocaine and bupivacaine is not an indicated usage of either anesthetic, although such a usage has become a common practice. Physicians should be aware of the potential incompatibility of the drug and synovial fluid.

Special Event

Touching Hands Project and the American Society for Surgery of the Hand (ASSH)

As the current President of the ASSH, Philadelphia Shiners Chief of Staff, Dr. Scott Kozin, has made it his goal for the Hand Society to become more involved in international outreach. Below is an excerpt from his mission statement and a link to the website for those interested in contributing their time or financial support. Personally, I have seen Dr. Kozin's presentation for the Touching Hands Project at both the ASSH and the AAHS meetings this year and felt particularly moved by his mission. Take a second to check out the mission and spread the word!

Rick Tosti, MD

<http://www.assh.org/Professionals/AboutASSH/OurFoundation/AFSHFundedPrograms/Pages/Touching-Hands-Project.aspx>



THE TOUCHING
HANDS PROJECT



The mission of the American Foundation for Surgery of the Hand is to advance the care of hand and upper extremity disorders by supporting education, research and outreach through the efficient collection of donations and administration of grants.

The Touching Hands Project (THP) was initiated in 2013 as part of the American Foundation for Surgery of the Hand (AFSH) with the goal of extending the mission into outreach to contribute to the healthcare of underserved populations. In addition, adding outreach is a tangible way to engage ASSH members, providing an avenue for donations of both financial support and service.

The medical advisory board (MAB) and ASSH council has decided that the initial endeavor of THP requires collaboration with an established and experienced organization devoted to outreach. The American Society for Surgery of the Hand (ASSH) would provide the hand surgery resource and the established organization would provide the infrastructure and the “boots on the ground” to ensure safety and success for our members.

The MAB explored numerous potential organizations for collaboration. The field was narrowed to the Adventist Hospital and Partners in Health (PIH) in Haiti. Other future collaboration includes Guatemala Healing Hands (GHH) and Cure International. All of these organizations were enthusiastic about collaboration with the ASSH.

The MAB decided that the inaugural collaboration would be with Adventist Hospital in Haiti. The goal is to have the first mission in May 2014. Adventist Hospital is uniquely positioned for collaboration with ASSH and hand surgery. The hospital has an ongoing relationship with the Foundation for Orthopedic Trauma (a subsidiary of Orthopedic Trauma Association devoted to outreach). The hospital provides ample infrastructure and volumes of patients that need hand and upper extremity treatment. In addition, Christophe Mackenson serves as the volunteer coordinator and Francel Alexis, MD is the Chief of Orthopedics, both dedicated to improving the care of Haitians.

To accomplish this task, the THP is seeking financial support from ASSH members and corporate partners. The goal is to increase the outreach corpus, such that the monies to support THP will be generated by interest on the monies raised. The goal is to make the outreach portion of the THP self-sufficient.

We hope you consider this request in the spirit of outreach, a noble goal for the ASSH. This initiative represents an objective that would increase our impact around the world and within the global hand community. THP represents a potential legacy that would propel the ASSH into the future.

Scott H. Kozin, MD; Peter Weiss, MD; Jennifer Wolf, MD

Special Event

The Formation of the Temple Hand Society

On a dark and cool Thursday evening in the Alamo Square district of San Francisco, California, Temple Ortho Alumni Abtin Foroohar and Asif Ilyas were meeting to conjure the next great society of orthopaedic surgeons: The Temple Hand Society. Their mission: to encourage an annual get-together on the Thursday night of the American Society for Surgery of the Hand (ASSH) meeting.

As the first acting President, Abi Foroohar invited all Temple alumni who perform surgery on the hand to begin a new tradition of dinner, drinks, and good company to be had wherever the ASSH meeting takes place. Dr. Foroohar, elected to a three-year term as President, said “traditionally, surgeons will meet for a fellowship alumni reception on the Friday night of the meeting; it would be nice to stay in touch and discuss cases, meet at the annual ASSH meeting, and generally socialize.” Member-at-large, Asif Ilyas, noted that “there are a growing number of hand surgeons who are also Temple Ortho alumni.” The goals going forward are to expand the club into a list-serve that is available for networking and discussion of difficult cases.

The first meeting of the Temple Hand Society was a smashing success. The inaugural group hailed Temple hand surgeons from both the East and West coasts (see photo below). “Next year, we hope to expand, find more of our long lost alumni, and continue to have a great Thursday night!” said President Foroohar.

For more information about the Temple Hand Society, email Abi Foroohar at: aforoohar@gmail.com.

For more information on the ASSH Meeting 2014 in Boston, visit: <http://asshannualmeeting.org/>.

Rick Tosti, MD



Inaugural members: (Front Row) Allen Tham (and Mrs. Tham), Abi Foroohar, Wade Andrews, Irfan Ahmed, Brian George, John Fowler, Alyssa Schaffer, Asif Ilyas; (Back Row) Kate Criner and Rick Tosti

Special Event

The Howard H. Steel Lecture at the Philadelphia Orthopaedic Society

Presented by:

DR. ALVIN H. CRAWFORD
Professor Emeritus, University of Cincinnati

“Pediatric Orthopaedics — My Journey”

This last year saw another fantastic installment of the annual Howard H. Steel Pediatric Lecture. After a fitting introduction by Program Chair Dr. Lawrence Wells, Dr. Alvin Crawford recounted his unique and storied experiences through both his and the field of pediatric orthopedics, past to present. In the end, he offered humbling advice to all of the residents in attendance in pursuing a path to becoming a greater physician, surgeon, and caregiver while keeping the importance of family and friends close to heart. The Howard Steel Pediatric Lecture ended with a rousing round of applause and ovation for both the guest speaker and the great man for which the lecture was named.

Colin Mansfield



Temple residents and Dr. Steel enjoying post-lecture discussions: (l-r) Drs. Colin Mansfield, Rich Han, Howard Steel, James Bennett, Emeka Nwodin and Anastassia Persidsky

Special Event

A Summary of this Year's National Hand Meetings

**American Society for Surgery of the Hand Meeting
October 2013 — San Francisco, California**

**American Association for Hand Surgery Meeting
January 2014 — Kauai, Hawaii**

Temple had some great success at the two major hand surgery meetings this academic year. The American Society for Surgery of the Hand (ASSH) met in San Francisco this past October under the theme “Education Through Technology.” The meeting highlighted several cutting edge techniques, instructional course lectures, and new technologies that are entering our field. Additionally, the symbolic torch was passed to Dr. Scott Kozin, of Shiners Hospital in Philadelphia, who was recently elected President for 2014. Dr. Kozin showcased his vision for the Hand Society during his presentation for the “Touching Hands Project,” which is a new outreach program to improve health care and hand deformities in underserved regions such as Haiti.

Temple had a unique opportunity to shine, as Rick Tosti and Asif Ilyas won the Julian M. Bruner award for “Best Poster” entitled “Prospective Evaluation of Pronator Quadratus Repair Following Volar Plating of Distal Radius Fractures.” The award came with a special display at the meeting, a monetary award, and a plaque. The ASSH also intends to share our poster at their exhibit at the 2014 American Academy of Orthopaedic Surgeons and the 2014 Orthopaedic Research Society Meetings in New Orleans, LA.

Temple also made its presence known at the American Association for Hand Surgery Meeting in Kauai, Hawaii. Rick Tosti and Temple Alumni John Fowler, Kris Matullo, and Asif Ilyas all took the podium for primary research presentations. Rick Tosti and Alyssa Schaffer had two poster presentations entitled “Prospective Evaluation of Vitamin D Levels in Young Adults With and Without Distal Radius Fractures” and “Emerging Multi-drug Resistance in MRSA Hand Infections.”

Rick Tosti



Rick Tosti and Asif Ilyas at the American Association for Hand Surgery in Hawaii

Resident Research Day

April 27, 2013

Presented in conjunction with Grand Rounds speaker

DR. VOLKER MUSAHL

Associate Professor, Orthopaedic Surgery Division of Sports Medicine, University of Pittsburgh

“How to Improve Outcome After ACL Reconstruction”

Once again, we had a successful and well-attended Resident Research Day. This year was prefaced with a Grand Rounds talk by Dr. Musahl and his work using motion tracking technology to follow ACL reconstruction outcomes. A lively discussion followed, rounded out by the presentations of a variety of this year’s Temple resident research projects. An impressive amount of time, energy and commitment was evident throughout the morning after hearing the talks, for which the department can be proud. A brief intermission was allowed while the judging took place, and congratulations to all of those who participated were espoused.

The following is a list of our top three winners. Special recognition was also given to them at the Alumni Day Banquet, where again they were able to show their research pursuits to our many alumni in attendance.

1. Kate Criner:

“Impact of statins on postoperative venous thromboembolic events following total knee and hip replacements”

2. Scott Barbash:

“Near infrared spectroscopy differentiates tendon and ligament composition”

3. Justin Iorio:

“Does Amicar affect blood loss in patients with adolescent idiopathic scoliosis treated with pedicle screws and Ponte osteotomies?”

Colin Mansfield

Special Event

Temple-Shriners Alumni Day

On a rainy Friday this past May 2013, the Temple University Hospital Department of Orthopaedics and Sports Medicine held its annual Temple-Shriners Alumni meeting at the Lulu Country Club. Although a little soggy, the day brought with it warm weather, great golf and a long line of Temple's best and brightest.

The event began with lectures given by distinguished Temple alumni. Topics included "Traumatic Instability of the Elbow" by Rob Kaufmann, MD, "Motion Preservation Options for Spondylolysis" by Paul Lin, MD and "Arthritis of the Ankle" by Chris Kestner, MD. These talks were followed by a point-counter point debate on the "Current Concepts in Surgical Treatment of Distal Radius Fractures" by Drs. Rob Kaufmann and his fellow (and Temple alumnus) at the University of Pittsburgh, John Fowler.

Next, the recipients of the Resident Research Award — Kate Criner (1st place), Scott Barbash (2nd place) and Justin Iorio (3rd place) — had the honor of re-presenting their works from Research Day.

The legendary Donald Ross designed golf course served as the perfect backdrop for several alumni and resident foursomes. These surgeons-turned-golfers competed for awards but mainly rekindled friendships beyond the walls of the operating room.

Arianna Trionfo

Special Event

Temple Ortho Tough Mudder

June 1, 2013

Jaindl Farms, Rural PA

A moment of inspiration came upon the Temple Orthopedics Department, an idea hatched in the depths of wintery flurries and pounding nor'easters: to sign up a team for the grueling and infamous Tough Mudder Run. A 10-mile bone and muscle crunching trek over, under and through a series of herculean obstacles made from mud, water, fire and glacier ice pits, and did I mention mud? If that wasn't enough to test the soul, several obstacles such as the one pictured above included electrical wires through which to navigate. The Temple Tough Mudder team met this challenge with vigor, and over a course of several months, trained for this event with the same tenacious and hard-working mentality that comes with being in the Temple Orthopedics family. Often in late night or early morning hours, each member sacrificed to prepare for this event, and it showed through the sweltering 80 degree day. And at the finish line, our team of eight made it through as one. When someone fell, there was a hand to pick them up. Whatever the trail had thrown at us, it was accomplished as a group. Staying true to 'Temple Tough,' we elected to finish the race as a linked unit: one-for-all through the live wires, and involuntary releases notwithstanding, we finished the day together as we started and for which we should be proud — as the Temple Orthopedics Team.

Colin Mansfield



Left to right: Drs. Sam Popinchalk, Matt Kleiner, Dustin Greenhill, Rupam Das, Colin Mansfield, J. Milo Sowards, Rick Tosti and Chris Haydel

Special Event

Fives Dominate Fours and Threes Earning Ponderosa Bowl Title 70-42

December 22, 2013

Sunday, December 22, 2014 marked the third annual Ponderosa Bowl. Formerly known as the “Shrine Bowl,” this year marked another major improvement to the annual football tradition — the game was played on a Sunday.

Despite a sub-optimal turnout, this three-on-three matchup was high paced and high scoring. The Red Team was comprised of Sam Popinchalk, MD, Emeka Nwodim, MD, and Rich Han, MD from the fifth-year resident class. The White Team consisted of Rick Tosti, MD from the fourth-year class, and Rupam Das, MD and Colin Mansfield, MD from the third-year class. Chris Haydel, MD represented the attendings with an outstanding all-time-offensive performance. Dr. Thoder provided another impeccable performance as head referee.

The Fives wasted no time scoring on their first drive. In fact, they wasted no time and continued to score on every subsequent drive. Fans were overheard saying “they look like men amongst boys,” and “a Ponderosa Bowl Hall of Fame should be created to remember this team,” and “who knew that Sam would have such a deadly accurate cannon for an arm?” and “I think Rupam has thrown as many pick-sixes as Sam has thrown touchdown passes,” and “Is that Colin coming in an hour late and why is he wearing a horse-head mask?”

The MVP award for this game was unanimous — Chris “Megatron” Haydel, MD. Chris was the prime target for quarterbacks on both sides in his all time-offensive standout performance. He ran more routes than anyone that day, demonstrating an athletic and cardiovascular capability that, quite frankly, surprised us all. Honorable mention goes to Rick Tosti, MD. Except for all of the plays that Emeka got by him for touchdowns, Rick was a “shut-down corner.” Overall, it was a hard fought competition with moments of brilliance from all participants.

Fortunately, there were no injuries to report. Few escape ventures that far outside of their envelope of activity unscathed. I personally scheduled an anticipatory Achilles tendon repair with Dr. Eremus for the Monday following the game. I cancelled my surgery and my workers compensation claim.

As the game ended, the Red Zone began in the recently renovated basement of the Ponderosa. As we all know so well, Dr. Thoder knows how to throw a party. All enjoyed food, beer, cigars, NFL football, darts, pool, and an all around great time. Sunday game day will be a lasting part of the tradition.

Sam Popinchalk, MD

Faculty

Temple University Department of Orthopaedic Surgery and Sports Medicine

Chairman

Joseph Thoder, MD, *The John W. Lachman Professor*

Professors

William DeLong, MD

Pekka Mooar, MD

Ray Moyer, MD, *The Howard H. Steel Professor*

Joseph Torg, MD

F. Todd Wetzel, MD, *Vice Chairman*

Associate Professors

Easwaran Balasubramanian, MD

Saqib Rehman, MD

Bruce Vanett, MD

Albert Weiss, MD

Assistant Professors

Joseph Eremus, MD

Christopher Haydel, MD

Eric Kropf, MD

Matthew Lorei, MD

Stanley Michael, MD

Alyssa Schaffer, MD

J. Milo Sowards, MD

Adjunct Faculty — Philadelphia Shriners Hospital

Scott Kozin, MD, *Chief of Staff*

Randal Betz, MD, *Emeritus Chief of Staff*

Philip Alburger, MD

Patrick Cahill, MD

Richard Davidson, MD

Corinna Franklin, MD

Howard Steel, MD, *Emeritus Chief of Staff*

Joshua Pahys, MD

Amer Samdani, MD

William Schrantz, MD

Harold van Bosse, MD

Daniel Zlotolow, MD

Adjunct Faculty — Abington Memorial Hospital

Andrew Star, MD, *Chief of Orthopaedics*

Shyam Brahmabhatt, MD

David Craft, MD

Matthew Craig, MD

Greg Galant, MD

Michael Gratch, MD

Victor Hsu, MD

Moody Kwok, MD

Guy Lee, MD

Thomas Peff, MD

T. Robert Takei, MD

Jeffrey Vakil, MD

Adjunct Faculty — St. Christopher's Hospital for Children

Peter Pizzutillo, MD, *Chief of Orthopaedics*

Kiersten Arthur, MD

Alison Gattuso, DO

Martin Herman, MD

Michael Kwon, MD

Juan Realyvasquez, MD

Joseph Rosenblatt, DO

Shannon Safier, MD

Michael Wolf, MD

Temple University Hospital
Department of Orthopaedic Surgery and Sports Medicine
Faculty 2013–2014



Joseph Thoder, MD
John W. Lachman Professor
Chairman
Hand & Upper Extremity
General Orthopaedics



J. Milo Sowards, MD
Sports Medicine



Easwaran Balasubramanian, MD
Joint Reconstruction
General Orthopaedics



Joseph Eremus, MD
Foot and Ankle
General Orthopaedics



Christopher Haydel, MD
Orthopaedic Trauma
General Orthopaedics



Cory Keller, DO
Sports Medicine



Eric Kropf, MD
Sports Medicine
General Orthopaedics



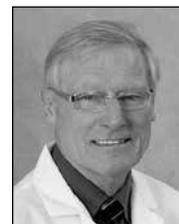
Matthew Lorei, MD
Joint Reconstruction
General Orthopaedics



Stanley Michael, MD
Sports Medicine
Joint Reconstruction
General Orthopaedics



Pekka Mooar, MD
Sports Medicine
Joint Reconstruction
General Orthopaedics



Ray Moyer, MD
Howard Steel Professor
Sports Medicine



Saqib Rehman, MD
Orthopaedic Trauma
General Orthopaedics



Alyssa Schaffer, MD
Hand Surgery



Joseph Torg, MD
Sports Medicine



Bruce Vanett, MD
General Orthopaedics



Albert Weiss, MD
Hand & Upper Extremity
General Orthopaedics



F. Todd Wetzel, MD
Vice-Chairman
Spine Surgery



Temple University Hospital

Department of Orthopaedic Surgery and Sports Medicine

House Staff 2013–2014



Scott Barbash, MD
PGY-5



Richard Han, MD
PGY-5



Emeka Nwodin, MD
PGY-5



Samuel Popinchalk, MD
PGY-5



Stephen Refsland, MD
PGY-4



Craig Steiner, MD
PGY-4



Rick Tosti, MD
PGY-4



Justin Iorio, MD
PGY-4



Rupam Das, MD
PGY-3



Colin Mansfield, MD
PGY-3



Kazimierz Komparda, MD
PGY-3



Mark Solarz, MD
PGY-3



Dustin Greenhill, MD
PGY-2



James Lachman, MD
PGY-2



Anastassia Persidsky, MD
PGY-2



Ariana Trionfo, MD
PGY-2



James Bennett, MD
PGY-1



Katharine Harper, MD
PGY-1



John Jennings, MD
PGY-1



William Smith, MD
PGY-1

Temple University Department of Orthopaedic Surgery and Sports Medicine: Research Update 2013–2014

Awards

- “Highlighted Poster” for Hand and Wrist Guided Poster Tours at the American Academy of Orthopaedic Surgeons Annual Meeting 2014. Tosti R, Samuelsen B, Bender S, Gaughan J, Schaffer AA, Ilyas AM. Emerging multi-drug resistance of methicillin resistant staphylococcus aureus in hand infections.
- “Julian M. Bruner Award for Best Poster of the ASSH” at the American Society for Surgery of the Hand Annual Meeting 2013. Tosti R, Ilyas AM. Prospective evaluation of pronator quadratus repair following volar plate fixation of distal radius fractures
- “Best Poster” for Hand and Wrist section of American Academy of Orthopaedic Surgeons Annual Meeting 2013. Fowler JR, Maltenfort M, Ilyas AM. Ultrasound as a First Line Test in the Diagnosis of Carpal Tunnel Syndrome: A Cost-effectiveness analysis.

Podium Presentations

- Tosti R, Samuelsen B, Bender S, Gaughan J, Schaffer AA, Ilyas AM. Emerging multi-drug resistance of methicillin resistant staphylococcus aureus in hand infections. Alternate paper presentation at *American Academy of Orthopaedic Surgeons Annual Meeting*, New Orleans, LA, March 2014
- Tosti R, Ilyas AM. Prospective evaluation of pronator quadratus repair following volar plate fixation of distal radius fractures. Presented at the *American Association for Hand Surgery Annual Meeting*, Kauai, HI, January 2014.
- Tosti R. Do povodone-iodine soaks reduce the number of operations needed to treat hand infections? Presented at the *American Association for Hand Surgery Annual Meeting*, Naples, FL, January 2013.
- Dakwar E, Bennett JT, Samdani AF. Case Presentation: Treatment of Spinal Deformity and Diastematomyelia with Vertebral Column Resection. *48th Annual Scoliosis Research Society Meeting*, Lyon, France, September 18–21, 2013.
- Singla A, Samdani AF, Flynn J, Bennett JT, Miyanji F, Pahys J, Marks M, Lonner B, Newton P, Cahill P, Betz RR. What is Different About Surgically Treated AIS Patients Who Achieve a Minimal Clinically Important Difference (MCID) in Appearance at 5 Years Post Surgery? *48th Annual Scoliosis Research Society Meeting*, Lyon, France, September 18–21, 2013.
- Singla A, Samdani AF, Sponseller P, Bennett JT, Pahys J, Marks M, Lonner B, Newton PO, Miyanji F, Betz RR, Cahill P. Selective Thoracic vs. Non-Selective Fusion in Lenke 3 Curves. *SRS 20th International Meeting on Advanced Spine Techniques*, Vancouver, British Columbia, July 10–13, 2013.
- Feuer G, Bennett JT, Saha S, Mijares D. Shear Properties of Cancellous Bone from Osteoporotic Sheep Treated with Synthetic Bone Mineral. *39th Annual Northeast Bioengineering Conference*, Syracuse, NY, April 5–7, 2013.
- Bennett JT, Samdani AF, Hoashi JS, Ames RJ, Kimball JS, Pahys JM. The Posterior Pedicle Screw Construct: 5 year results for thoracolumbar and lumbar curves. *AANS/CNS Disorders of the Spine and Peripheral Nerves 29th Annual Meeting*, Phoenix, AZ, March 6–9, 2013.
- Bennett JT, Samdani AF, Belin E, Pahys J, Shah SA, Newton PO, Betz RR, Sponseller PD. Major Perioperative Complications after Surgery for Cerebral Palsy: Assessment of risk factors. *AANS/CNS Disorders of the Spine and Peripheral Nerves 29th Annual Meeting*, Phoenix, AZ, March 6–9, 2013.
- Bennett JT, Samdani AF, Belin E, Pahys JM, Marks M, Miyanji F, Cahill P, Shufflebarger H, Lonner B, Newton PO, Betz RR. Unplanned Return to the Operating Room in Patients with AIS: Are we doing better with pedicle screws? *AANS/CNS Disorders of the Spine and Peripheral Nerves 29th Annual Meeting*, Phoenix, AZ, March 6–9, 2013.
- Bennett JT, Ames RJ, Samdani AF, Garg H, Cahill PJ, Miyanji F, Lonner B, Marks MC, Betz RR, Newton PO. 5 Year Results for Lenke 1 and 2 Curves: Comparison of anterior, posterior hybrid, and posterior all pedicle screws. *AANS/CNS Disorders of the Spine and Peripheral Nerves 29th Annual Meeting*, Phoenix, AZ, March 6–9, 2013.

Poster Presentations

- Tosti R, Samuelsen B, Bender S, Gaughan J, Schaffer AA, Ilyas AM. Emerging multi-drug resistance of methicillin resistant staphylococcus aureus in hand infections. *American Academy of Orthopaedic Surgeons Annual Meeting*, New Orleans, LA, March 2014.
- Star A, Han R. Vascular Complications in Total Knee Arthroplasty: A Newly Recognized Complication and Lessons from our Practice. *American Academy of Orthopaedic Surgeons Annual Meeting*, New Orleans, LA, March 2014.
- Criner K, Trionfo A. Impact of Statins on Postoperative Venous Thromboembolic Events Following Total Knee and Hip Replacements. *American Academy of Orthopaedic Surgeons Annual Meeting*, New Orleans, LA, March 2014.
- Tosti R, Ilyas AM. Prospective evaluation of pronator quadratus repair following volar plate fixation of distal radius fractures. American Society for Surgery of the Hand: Julian M. Bruner Award Exhibit at the *American Academy of Orthopaedic Surgeons Annual Meeting*, New Orleans, LA, March 2014.
- Tosti R, Samuelsen B, Bender S, Gaughan J, Schaffer AA, Ilyas AM. Emerging multi-drug resistance of methicillin resistant staphylococcus aureus in hand infections. *American Association for Hand Surgery Annual Meeting*, Kauai, HI, January 2014.
- Tosti R, Atiemo E, Jennings J, Baker J, Gaughan J, Mooar P, Schaffer AA, Ilyas AM. Prospective evaluation of vitamin D levels in young adults with and without low energy distal radius fractures. *American Association for Hand Surgery Annual Meeting*, Kauai, HI, January 2014.
- Tosti R, Ilyas AM. Prospective evaluation of pronator quadratus repair following volar plate fixation of distal radius fractures. *American Society for Surgery of the Hand Annual Meeting*, San Francisco, CA, October 2013.
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Grand Rounds 2013–2014

Wednesday, August 21, 2013

7:00–7:45 Pain Management in Orthopaedics — Gary Trehan, MD

7:55–8:15 Postoperative Disposition of the Opioid Dependent Patient — Samuel Popinchalk

Saturday, September 14, 2013

8:00–8:45 Current Concepts in ACL Injuries — Shyam Brahmabhatt

8:55–9:15 Evolution of Tommy John Surgery — Rick Tosti

Wednesday, September 25, 2013

7:00–7:45 Historical and Practical Notions About Osteomyelitis — Peter Axelrod

7:55–8:15 Local Antibiotic Treatment of Bone and Joint Infections: Current Evidence — Richard Han

Wednesday, October 16, 2013

7:00–7:45 The Subscapularis: Keystone of the Shoulder or Red-Headed Stepchild? — J. Milo Sowards

7:55–8:15 Long Head of the Biceps Tendon Pathology — Justin Iorio

Saturday, November 2, 2013

8:00–8:45 Osteoporosis: What Every Orthopaedic Surgeon Should Know(!) and Do(?) — Asif Ilyas

8:55–9:15 Acute Vascular Injury in the Hand and Forearm — Scott Barbash

Wednesday, November 13, 2013

7:00–7:45 Selected Topics in Pediatric Sports — Corinna Franklin

7:55–8:15 Shoulder Instability in Children — Emeka Nwodim

Wednesday, December 11, 2013

7:00–7:45 Pediatric Musculoskeletal Infection Update: MRSA and a New Paradigm for Treatment
— Martin Herman, MD

7:55–8:15 Professionalism — Kazimierz Komperda

Saturday, January 4, 2014

8:00–8:45 What Do We Really Know About Picking a “Good” Orthopaedic Resident — Alyssa Schaffer

8:55–9:15 Is 80 Hours Enough? The Evolution of the Duty Hour Regulations — Rupam Das

Wednesday, January 15, 2014

7:00–7:45 Healthcare Changes in the Horizon — What the Orthopaedic Surgeon Needs to Know
— Rob Purchase/John Cacciamani

7:55–8:15 Medical Student Debt and Its Effect on Career Choice — Mark Solarz

Wednesday, February 12, 2014

7:00–7:45 Non Arthritic Hip: Evaluation, Management, and Joint Preservation Surgery — Eric Kropf

7:55–8:15 Radiographic Evaluation of Hip Dysplasia Presenting in Adulthood — Stephen Refsland

Saturday, March 8, 2014

8:00–8:45 NATO Role 3 Kandahar, Afghanistan: My Orthopaedic Experience from a War Zone —
Carlos Moreyra, MD

8:55–9:15 Management Update on Patellar Instability — Colin Mansfield

Snapshots from 2013–2014



The Orthopaedic “Soup and Bowl” hosted by Dr. Eremus and the Merion Cricket Club



Temple Ortho Tough Mudder Team (before the mud)



“Two attendings and six residents started; eight teammates finished!” — J. Milo Sowards



When doctors are ill they don’t take sick days . . . they get IV fluids in between cases!



Dr. Lorei and Rick Tosti shop at the same store



Sideline docs at Heinz Field

Snapshots from 2013–2014



Dr. Thoder's classic carpal instability lecture



Cardiac Surgery Appreciation Day... they do have impeccable style!



Pulmonary and Critical Care Appreciation Day: function over fashion!



Trauma team dinner extravaganza



The chiefs after a long day of operating



Dr. Vanett rallying the team

Snapshots from 2013–2014



How does a Polish Orthopaedist read x-rays . . . ?



Dr. Swards uses the dinnerware as a musculo-skeletal visual aid



Joe Dwyer and Chris Haydel say “there is a fracture, I need to fix it!”



Colin Mansfield and Kasey Komperda at the arthroscopy course in Rosemont, IL



Dr. Thoder and Colin Mansfield help Arianna Trionfo celebrate her first reduction of a dislocated hip



Ever wonder what goes on in the orthopaedics call room?

Snapshots from 2013–2014



Asif Ilyas, Alyssa Schaffer, and Rick Tosti enjoying a nice adventure after a day of presenting Temple research at the AAHS meeting in Naples, Florida



At the Arthroscopy course in Rosemont, IL: Steve Refsland, Rick Tosti and McLovin! (really, the actor happened to be in Rosemont)



Steve Refsland at the AANA course getting his scope on



Interns working hard (well . . . maybe one of them)



Dustin Greenhill and Scott Barbash watching the master at work



Monocles and handlebar mustaches: true men of style

Instructions to Authors

Editorial Philosophy

The purpose of the *Temple University Journal of Orthopaedic Surgery & Sports Medicine (TUJOSM)* is to publish clinical and basic science research performed by all departments of Temple University that relate to orthopaedic surgery and sports medicine. As such, *TUJOSM* will consider for publication any original clinical or basic science research, review article, case report, and technical or clinical tips. All clinical studies, including retrospective reviews, require IRB approval.

Editorial Review Process

All submissions will be sent to select members of our peer review board for formal review.

Manuscript Requirements

Manuscripts are not to exceed 15 double spaced type-written pages and/or 5,000 words (minus figures/tables/pictures). The manuscript should contain the following elements: Title page, Abstract, Body, References, and Tables/Legends. Pages should be numbered consecutively starting from the title page.

(1) Title Page — The first page, should contain the article's title, authors and degrees, institutional affiliations, conflict of interest statement, and contact information of the corresponding author (name, address, fax, and email address).

(2) Abstract — The second page, should be a one-paragraph abstract less than 200 words concisely stating the objective, methods, results, and conclusion of the article.

(3) Body — Should be divided into, if applicable, Introduction, Materials & Methods, Results, Discussion, and Acknowledgements. Tables and figures (in JPEG format) with their headings/captions should be listed consecutively on separate pages at the end of the body, not continuous within the text.

(4) References — Should be listed following the format utilized by *JBJS*. For example: Smith, JH, Doe, JD. Fixation of unstable intertrochanteric femur fractures. *J Bone Joint Surg Am.* 2002;84:3553–58.

Submissions

All submissions are now digital. Please submit the manuscript in a Microsoft Word document to templejournal@gmail.com.

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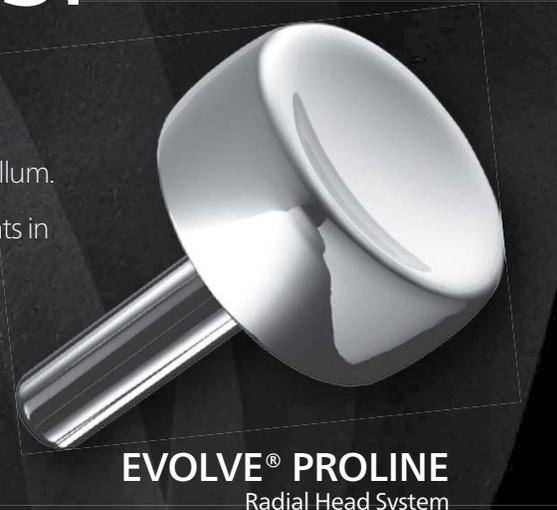
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1. Dai, et al., ORS 2013, San Antonio, TX, Influence of Ethnicity on Coverage of the Tibia in Total Knee Arthroplasty 2. Data on file at Zimmer

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