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Osteomyelitis Risk Factors Related to Combat Trauma Open Tibia Fractures: A Case-control Analysis

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Abstract

Objectives—We assessed osteomyelitis risk factors in U.S. military personnel with combat-related open tibia fractures (2003–2009).

Methods—Patients with open tibia fractures who met diagnostic criteria of osteomyelitis were identified as cases using Military Health System data and verified through medical record review. Controls were patients with open tibia fractures who did not meet osteomyelitis criteria. Gustilo-Andersen (GA) fracture classification scheme was modified to include transtibial amputations

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(TTAs) as the most severe level. Logistic regression multivariable odds ratios (OR; 95% confidence interval [CI]) were assessed.

Results—A total of 130 tibia osteomyelitis cases and 85 controls were identified. Excluding patients with TTAs, osteomyelitis cases had significantly longer time to radiographic union compared to controls (median: 210 versus 165 days). Blast injuries, antibiotic bead utilization, ≥GA-IIIb fractures (highest risk with TTA [OR: 15.10; CI: 3.22–71.07]) and foreign body at fracture site were significantly associated with developing osteomyelitis. In a separate model, the Orthopaedic Trauma Association Open Fracture Classification muscle variable was significant with increasing risk from muscle loss (OR: 5.62; CI: 2.21–14.25) to dead muscle (OR: 8.46; CI: 3.31–21.64). When TTAs were excluded, significant risk factors were similar and included sustaining an injury between 2003 and 2006.

Conclusions—Patients with severe blast trauma resulting in significant muscle damage are at the highest risk for osteomyelitis. The time period association coincides with a timeframe when several trauma system practice changes were initiated (e.g., increased negative pressure wound therapy, decreased high pressure irrigation, and reduced crystalloid use).

Level of Evidence—Prognostic Level III

INTRODUCTION

Orthopaedic injuries accounted for 82% of wounded personnel in Iraq and Afghanistan between 2001 and 2005, of which 53% were penetrating soft-tissue injuries and 26% were fractures.[1] Civilian and military trauma care are similar in including prompt antibiotic administration, wound debridement and irrigation, fracture and hemodynamic stabilization, timely wound closure or coverage, and rehabilitation. Nevertheless, the injury mechanism and environment are different for combat casualties. Blast injuries from high-energy improvised explosive devices (IEDs), which are uncommon in civilian trauma, result in extensive wound contamination and tissue loss.[2–5] Furthermore, the combat casualty care environment involves medical evacuation through multiple levels of care (i.e., combat zone facilities, regional hospitals outside combat zone, and United States hospitals for definitive treatment and rehabilitation).[6]

Although combat casualty care has improved during the last decade, infectious complications, including osteomyelitis, remain a frequent occurrence.[7–13] An evaluation of 664 combat casualties admitted to the orthopaedic service at Brooke Army Medical Center (2003–2006) found that 15% were diagnosed with osteomyelitis.[12] Moreover, among wounded United Kingdom (U.K.) military personnel with open tibia fractures, 23% developed deep infections.[14] In civilian cases, patients with open fractures frequently develop infections,[15–19] with severe tibia fractures (Type III) having rates as high as 35%.[20–25] Among combat casualties with Type III open tibia fractures, deep infections, including osteomyelitis, are associated with increased resource utilization stemming from revision surgeries and late amputations (≥12 weeks post-injury).[26]

There are a variety of factors that may contribute to a patient's outcome after an orthopaedic injury, and more specifically whether an infection develops.[26,27] Using a comprehensive review of data over a 6-year period and from multiple clinical sites, we assessed risk factors

for development of osteomyelitis in combat-wounded individuals with open tibia fractures, including transtibial amputations (TTAs).

METHODS

Study Population

Data were collected from U.S. service members with deployment-related orthopaedic trauma sustained from March 19, 2003 through December 31, 2009. Patients were medically evacuated from the combat theater to Landstuhl Regional Medical Center (Germany), and subsequently transferred to a U.S. military hospital: Walter Reed Army Medical Center (Washington, DC), National Naval Medical Center (Bethesda, MD), or Brooke Army Medical Center (San Antonio, TX). The study was approved by the Infectious Disease Institutional Review Board of the Uniformed Services University of the Health Sciences.

Case-Control Classification

The Military Health System Data Repository was surveyed for patients with International Classification of Diseases (9^{th} revision, Clinical Modification) codes related to lower extremity injuries. The Department of Defense Trauma Registry and Military Health System pharmacy, laboratory, and radiology records were also reviewed. Medical records from all potential subjects were independently reviewed by an infectious disease and orthopaedic surgery physician, using standardized criteria to verify case and control classifications. The study population was restricted to patients with trauma-related open tibia fractures. Using a modified version of the Gustilo-Anderson (GA) classification system, open fractures were categorized (at the discretion of the orthopaedic surgeon) into four grades: GA-I, GA-II, GA-III, as well as an additional category for traumatic and early surgical TTAs.[28] Fractures were classified in accordance with the Orthopaedic Trauma Association's (OTA) Open Fracture Classification (OFC) system.[29,30]

All cases were classified in accordance with the Centers for Disease Control and Prevention, National Healthcare Safety Network (NHSN) published grading of osteomyelitis diagnoses as definite, probable, or possible.[31] The NHSN definitions are utilized by state registries and surveillance systems,[32–34] as well as the European Centre for Disease Prevention and Control.[35] Definite osteomyelitis required either a positive bone culture or evidence of bone infection on direct examination during a surgical procedure or histopathological examination. A probable osteomyelitis was defined by occurrence of ≥2 of the following signs/symptoms (>38°C temperature, localized swelling, localized heat, localized tenderness, drainage at site) in addition to either organisms cultured from blood samples or radiographic evidence of infection. A possible osteomyelitis required environmental contamination at time of injury, deep wound tissue growing any organism, and evidence of either local (purulence or necrotic tissue at affected site) or systemic inflammation (>38°C temperature, ≥12,000 μL leukocytes, or elevated C-reactive protein or erythrocyte sedimentation rate). Patients with a fracture delayed union (or established nonunion) on follow-up examination with evidence of systemic inflammation were also considered to have a possible osteomyelitis. Inclusion in the control population required an open tibia fracture without meeting diagnostic criteria for osteomyelitis.

Statistical Analysis

Characteristics of patients with and without osteomyelitis were compared using Chi-square testing (or Fisher's exact test) for categorical variables and Wilcoxon rank-sum test for continuous variables. Potential risk factors for development of osteomyelitis were examined through univariable and multivariable logistic regression models. Covariates with a p-value ≤0.2 in the univariable model were considered for inclusion in the multivariable model. Stepwise, backward, and forward model selections were conducted to choose the multivariable risk factor model. Risk factors with an overall p-value <0.05 were retained in the model.

RESULTS

Study Population

A total of 130 osteomyelitis cases and 85 controls were identified (Table 1). Patients were predominantly male (97%), injured in Iraq (86%), and sustained injuries between 2003 and 2006 (59%). A significantly greater proportion of osteomyelitis cases incurred injuries via a blast mechanism (82% versus 62%; p=0.001); however, there was no significant difference related to injury severity scores and blood transfusions within 24 hours post-injury between cases and controls. A higher proportion of patients injured in Iraq were from the earlier time period compared to Afghanistan (62% versus 40%; p=0.022), due to casualty rates from the respective operational theaters.

Clinical and Open Fracture Characteristics

Among the osteomyelitis cases, 25 (19%) met the definition for either definite or probable, while the remaining 105 (81%) met criteria for a possible osteomyelitis. Except for a higher proportion of localized site swelling among definite/probable cases compared to possible, there was no significant difference between the classification groups regarding clinical presentation for local signs and symptoms (data not shown). Regarding systemic inflammation, the median maximum temperature was 38.7°C (interquartile range [IQR]: 37.8–39.4°C) for definite/probable and 38.9°C (IQR: 38.3–39.4) for possible cases. The median maximum white blood cell count was 17.8 (interquartile range [IQR]: 12.3–19.6) for definite cases, 17.4 (IQR: 13.7–24.5) for probable cases, and 18.8 (IQR: 13.9–25.1) for possible cases. For definite cases, the median maximum C-reactive protein level was 13.3 (IQR: 5.4–23.8), while it was 15.2 (IQR: 8.5–17.7 for probable cases and 16.1 (IQR: 8.6–22.5) for possible cases. Lastly, erythrocyte sedimentation rate was a maximum median value of 90.5 (IQR: 78–115.5), 97 (IQR: 76–120), and 113 (IQR: 93–120) for definite, probable, and possible cases, respectively.

Information on timing of first operating room visit in theater was available for 74 patients, of which 85% were seen within the first 6 hours post-injury (95% seen within 24 hours). The majority of subjects (81%) recovered Gram-negative bacteria with the predominant organism across the definite/probable and possible cases being *Acinetobacter calcoaceticus baumannii* complex (44% and 56%, respectively).

Using the modified GA fracture classification, significantly more osteomyelitis cases had GA-IIIb fractures and TTAs ($p<0.001$; Table 2). Regarding the OTA OFC for skin, muscle, bone loss, and contamination variables, osteomyelitis cases had more extensive degloving, dead muscle, loss of muscle function, or partial/complete muscle excision, segmental bone loss, and contamination embedded in bone or deep soft-tissue ($p\leq0.001$).

Management and Outcomes

Excluding TTAs, the first type of orthopaedic hardware for the majority of cases and controls involved external fixation of the tibia/fibula (91% and 90%, respectively; Table 3). In contrast, there was a significant difference in the last type of orthopaedic hardware with osteomyelitis cases having a higher proportion of external fixation (68%) compared to controls (33%; $p<0.001$). A greater amount of osteomyelitis cases were treated with antibiotic beads (approximately 82% vancomycin; 18% tobramycin or composition not stated) compared to controls ($p<0.001$). Information on use of prophylactic antibiotics within 48 hours post-injury in the combat theater was lacking for 77% of subjects and, thus, not included in the analysis.

Osteomyelitis cases had a significantly longer duration to final stabilization (>6 months post-injury for 44% versus 30%; $p=0.002$; Table 3). Median time to radiographic union was 210 days for osteomyelitis cases and 165 days for controls ($p=0.014$).

Case-Control Risk Analysis

Blast injury, GA-IIIa and higher fracture class, TTAs (traumatic and early surgical), OTA OFC variables, use of antibiotic beads, and presence of foreign body at bone site (fragment and/or hardware) were significantly associated with risk of osteomyelitis in the univariable model (Table 4). Due to high correlation between GA fracture classification and OTA OFC variables, the two classification schemes warranted separate multivariable assessments (Table 5). In the multivariable model including GA fracture classification, sustaining a blast injury, receiving a classification of GA-IIIb or higher, use of antibiotic beads, and presence of a foreign body fragment at tibia site (with/without hardware) were independently associated with osteomyelitis risk. Traumatic or early surgical TTA prior to infection incurred the highest risk. In the OTA OFC model, use of antibiotic beads remained a significant risk factors and the OTA OFC variable related to muscle loss showed an increasing risk of osteomyelitis.

Restricted analyses excluded patients with TTA, leaving 89 osteomyelitis cases and 72 controls (Tables 4 and 5). In both the GA classification and OTA OFC variable models, being injured between 2003 and 2006, sustaining a blast injury, and use of antibiotic beads were independent risk factors for developing osteomyelitis (Table 5). In the GA classification model, the level of GA-IIIb was significantly associated with osteomyelitis risk; however, GA-IIIc was not. Similar to the prior model, the OTA OFC variable related to muscle loss was an independent risk factor.

DISCUSSION

Trauma-associated osteomyelitis in this severely injured population is a significant complication given the high frequency of blast trauma resulting in severe open fractures and/or amputations, as well as the frequent contamination of wounds. While our analysis does have inherent limitations, it provides a systematic investigation of factors associated with osteomyelitis risk in a unique patient population. Our analysis found that blast injuries, severity related to open tibia fractures, sustaining an injury between 2003 and 2006, as well as presence of a foreign body at the tibia fracture site, were also risk factors.

The highest risk of developing osteomyelitis was traumatic or early surgical TTAs (Table 5), most frequently associated with IED blast injuries. Having a foreign body fragment (with/without hardware) at the tibia site was also a risk factor and likely results from IED shrapnel. Although risk factors were not assessed, a recent analysis of open tibia fractures among wounded U.K. military personnel found degree of bone loss was significantly associated with infections.[14] In our analysis, a significantly higher proportion of segmental bone loss was observed among osteomyelitis cases and while it was significant in the univariable model, the variable was not retained in the multivariable model.

By excluding patients with TTA, the multivariable model assessed characteristics of a population of open fracture patients more comparable to civilian trauma patients. Similar to the full model, OTA OFC for muscle loss remained an independent predictor, indicating high importance of soft-tissue injury severity as related to risk of osteomyelitis. This finding corresponds to a recent analysis of open tibia fractures among civilian patients that identified soft-tissue injury (suggestive of muscle damage/loss) as the most important infection risk factor.[25] In our analysis, GA-IIIb fracture classification was also associated with osteomyelitis risk; however, GA-IIIc was not. This is possibly due to limited statistical power as there were only 22 patients with a GA-IIIc classification in our population.

Among civilian trauma patients, fracture classification of GA-IIIa or higher, occurrence of at least one immune comprising condition, and injury location have been identified as independent predictors of osteomyelitis.[36] In addition, a recent analysis of 486 patients with open tibia fractures confirmed significance of GA-III fracture classification with infection risk. Specifically, there were a 9.3, 25.4, and 108.9 times more likely risk to become infected with GA-IIIa, GA-IIIb, and GA-IIIc fractures, respectively.[25] These data corroborate our findings that infection risk increases with severity of fracture/traumatic TTA. Specifically, in our analysis, the largest proportion of infection was observed with patients classified as GA-IIIb (37 out of 51; 73%), which carried the highest risk after excluding TTAs (Table 5). Nevertheless, the OTA OFC may be a more accurate representation given that it more precisely accounts for soft-tissue injury severity and degree of contamination, with the highest proportion (56 out of 76; 74%) and risk associated with dead muscle (Table 5). One argument to reduce the high infection rate following TTAs would be to perform more proximal early amputations. Unfortunately, zones of injury following IED injuries are frequently massive and most patients have (at least) soft-tissue injuries proximal to the level of the tibial injury, making a “clean” amputation proximal to the injury impossible or requiring dramatic measures, such as hip disarticulations. Furthermore, despite the high

early infection rate, all TTA in our study were successfully salvaged at that level, resulting in maintenance of the native knee joint and ostensibly better lifelong function than might be afforded by knee disarticulations or transfemoral amputations.

The significant association with the earlier time period (2003–2006) correlates with changing U.S. military practice patterns and development of clinical practice guidelines for infection prevention in combat casualties.[37,38] At the start of the study period, use of high-pressure irrigation was standard practice for treatment of open wounds/fractures and a recent meta-analysis identified pulsatile lavage as an infection risk factor with open fractures (risk ratio: 2.70; 95% confidence interval: 1.03–7.05).[39] Around 2006–2007, use of pulsatile lavage decreased and negative pressure wound therapy became more frequent due to data demonstrating promotion of wound healing and reduction in infectious complications. Specifically, studies have shown that negative pressure wound therapy is associated with improved bacterial clearance, blood flow, and granulation tissue in the wounds, along with a reduction in edema, infections, and wound dehiscence.[37,40–42] Moreover, important changes in resuscitation occurred around the time period with more restricted use of crystalloid products and optimization of blood product transfusion (1:1 ratio of packed red blood cells and plasma).[43] Although not directly assessed, these changes lessening third space fluid may have impacted risk for late infection events. Regarding the association of osteomyelitis risk with use of antibiotic beads prior to infection diagnosis, the surgeon's decision to use antibiotic beads is based on appearance and severity of the wound, along with extent of defect. During the wars in Iraq and Afghanistan, IEDs were the predominant injury mechanism, resulting in grievous extremity injuries characterized by extensive soft-tissue and muscle damage.[44] Due to the nature of the injuries, risk of infection was high; therefore, it is probable that antibiotic beads were placed preferentially in more severe injuries which, in turn, were more prone to develop osteomyelitis. While use of antibiotics was not identified as risk factors in the recent meta-analysis, factors related to polytrauma and fracture severity were associated with infections,[39] which is consistent with our findings.

The recent meta-analysis examined a wide range of infection risk factors associated with open fractures.[39] Smoking was found to be associated with increased risk of infections;[39] however, it was not identified as an independent predictor in our analysis nor in the analysis of U.K. military personnel.[14] Prior analyses have examined the timing of antibiotic prophylaxis with regards to infections; however, Kortram et al.[39] found that osteomyelitis risk was not elevated when antibiotics were received >3 hours after injury (risk ratio: 1.29; 95% confidence interval: 0.59–2.79). Furthermore, blood transfusions have been shown to modulate the immune system and are associated with infection risk, including osteomyelitis.[6,39] Blood volume was not associated with osteomyelitis risk in this military population with battlefield injuries. Timing of surgical debridement was also examined as a risk factor. Guidelines recommend that surgical debridement occurs <6 hours for the management of open fractures. Precise timing of first operative procedure was available for 74 patients in our analysis with 85% having their first operating room visit <6 hours post-injury. In the recent meta-analysis, timing of debridement (>6 hours versus <6 hours) was not significantly associated with infection risk,[39] indicating delayed surgical debridement may not negatively impact morbidity. These findings confirmed the results of a separate meta-analysis, which compared data between patients with open tibia fractures who received early

(<6 hours) and late (>6 hours) surgical debridements and found no association between timing of debridement and rate of overall infections, deep infections, and nonunion.[45] While not significant as a risk factor in the meta-analysis,[39] external fixation has been associated with higher infection rates with GA-I and GA-II fractures, while it decreased likelihood of infections with GA-III fractures.[46] GA-III fractures comprised 84% of our population (excluding TTA) and while use of any external fixation was not significantly different between cases and controls (85% versus 78%, respectively), more cases did have external fixation as their last orthopedic hardware (68% versus 33%; $p<0.001$). The timing of wound closure has also been examined with occurrence of closure >5 days post-injury being identified as an infection risk factor with open tibia fractures.[47]

Our analysis does have several important limitations. In particular, the majority of our cases are classified as possible based on NHSN criteria, which could have allowed the inclusion of cases with deep soft-tissue infections (with or without osteomyelitis) in our analysis. This limitation stems from the inherent complexity of combat trauma resulting in open tibia fractures or amputations. Due to the retrospective nature of this analysis, we were limited to reviewing available medical records in which operative descriptions may lack the specificity required to classify an osteomyelitis as definite coupled with infrequent bone cultures and histopathology. In addition, due to the low number of patients with open tibia fractures who did not meet osteomyelitis diagnostic criteria, we were not able to match the case and control populations. Detailed information on use of early post-trauma antibiotics in the combat theater is lacking. Precise timing between injury and initial surgical care was unavailable for the majority of patients. Another limitation is the lack of available information on the timing of wound closure in our population. Furthermore, data in our analysis may not be applicable to general civilian trauma as the majority of the population sustained blast-related trauma. Lastly, patient-level data related to practice patterns (e.g., use of negative pressure wound therapy) is lacking.

Despite these limitations, our analysis demonstrates risk factors for osteomyelitis among combat casualties is highest with severe blast trauma resulting in substantial muscle loss/damage with the most extreme circumstances being trauma/early surgical TTAs. Time-dependent variables related to early care were not included in this analysis, but could represent important risk factors and should be evaluated in future research. Future research includes an evaluation of the risk of recurrent osteomyelitis based on initial classification, wound severity, microbiology, antibiotic therapy, and early surgical care.

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Table 1

Demographics and Injury Characteristics, No. (%), of Wounded Military Personnel with and without Tibia Osteomyelitis

	Total (N=215)	Osteomyelitis Cases (N=130)	Controls (N=85)	P-value
Male	209 (97.2)	125 (96.2)	84 (98.8)	0.407
Age at time of injury, median (IQR)	24 (21–30)	24 (21–31)	23 (21–29)	0.962
History of tobacco use[1]	89 (47.6)	59 (51.8)	30 (41.1)	0.178
Operational theater				0.045
Iraq	185 (86.0)	117 (90.0)	68 (80.0)	
Afghanistan	30 (14.0)	13 (10.0)	17 (20.0)	
Time period				0.258
2003–2006	127 (59.1)	81 (62.3)	46 (54.1)	
2007–2009	88 (40.9)	49 (37.7)	39 (45.9)	
Branch of service				0.345
Army	177 (82.3)	110 (84.6)	67 (78.8)	
Marine	31 (14.4)	18 (13.8)	13 (15.3)	
Air Force	3 (1.4)	1 (0.8)	2 (2.4)	
Navy	4 (1.9)	1 (0.8)	3 (3.5)	
Blast mechanism of injury	160 (74.4)	107 (82.3)	53 (62.4)	0.001
Blood product transfusions within first 24 hours				0.069
None or missing units	105 (48.8)	55 (42.3)	50 (58.8)	
1–9 units	65 (30.2)	44 (33.8)	21 (24.7)	
≥10 units	45 (20.9)	31 (23.8)	14 (16.5)	
Injury severity score[2]				0.523
0–9 (mild)	75 (34.9)	44 (33.8)	31 (36.5)	
10–15 (moderate)	83 (38.6)	54 (41.5)	29 (34.1)	
≥16 (severe to life-threatening)	57 (26.5)	32 (24.6)	25 (29.4)	

IQR - interquartile range

[1] Tobacco history was not known for 28 patients (16 cases and 12 controls). Percentages are based on total minus unknown.

[2] The Injury Severity Score is an overall measure calculated for each patient based on the top three maximum Abbreviated Injury Scale anatomical region values[48]

Table 2

Characteristics, No. (%), of Open Tibia Fractures Sustained by Military Personnel

	Total (N=215)	Osteomyelitis Cases (N=130)	Controls (N=85)	P-value
Fracture Class[1]				<0.001
GA-II	22 (10.2)	5 (3.8)	17 (20.0)	
GA-IIIa	62 (28.8)	32 (24.6)	30 (35.3)	
GA-IIIb	51 (23.7)	37 (28.5)	14 (16.5)	
GA-IIIc	22 (10.2)	13 (10.0)	9 (10.6)	
TTA[2]	54 (25.1)	41 (31.5)	13 (15.3)	
Open fracture not otherwise specified	4 (1.9)	2 (1.5)	2 (2.4)	
OTA OFC: Skin[3]				<0.001
Can be approximated	59 (28.8)	22 (17.5)	37 (46.8)	
Cannot be approximated	65 (31.7)	44 (34.9)	21 (26.6)	
Extensive degloving	81 (39.5)	60 (47.6)	21 (26.6)	
OTA OFC: Muscle[4,5]				<0.001
Grade I	40 (20.9)	9 (7.7)	31 (41.9)	
Grade II	75 (39.3)	52 (44.4)	23 (31.1)	
Grade III	76 (39.8)	56 (47.9)	20 (27.0)	
OTA OFC: Arterial[6]				0.065
No injury	135 (64.9)	74 (58.7)	61 (74.4)	
Injury without ischemia	10 (4.8)	7 (5.6)	3 (3.7)	
Injury with distal ischemia	63 (30.3)	45 (35.7)	18 (22.0)	
OTA OFC: Bone loss[7]				0.001
None	55 (26.4)	23 (18.1)	32 (39.5)	
Bone missing/devascularized with contact by proximal/ distal fragments	69 (33.2)	43 (33.9)	26 (32.1)	
Segmental bone loss	84 (40.4)	61 (48.0)	23 (28.4)	
OTA OFA: Contamination[8]				0.001
None or minimal	6 (2.9)	0	6 (7.4)	
Surface contamination	37 (18.0)	16 (12.8)	21 (25.9)	
Embedded in bone / deep soft-tissue	96 (46.6)	67 (53.6)	29 (35.8)	
High-risk environmental conditions	67 (32.5)	42 (33.6)	25 (30.9)	

TTA - transtibial amputation; OTA OFC - Orthopaedic Trauma Association's Open Fracture Classification

[1]Based on a modified Gustilo-Anderson (GA) classification.[28] There were no patients with GA-I fractures in the analysis.

[2]Amputation prior to infection. Among the osteomyelitis case TTAs, 31 were traumatic and 10 were from surgery prior to admission in the United States. All control TTAs were traumatic.

[3]There are 10 patients with unknown/missing classifications (4 cases and 6 controls). Percentages based on total minus unknown.

[4]Grade I - no muscle in area, no appreciable muscle necrosis, some muscle injury with intact function; Grade II - loss of muscle but function remains, some localized necrosis requiring excision, intact muscle-tendon unit; Grade III - dead muscle, loss of function, partial/complete excision, complete disruption of unit, defect does not approximated.

[5]There are 24 patients with unknown/missing classifications (13 cases and 11 controls). Percentages based on total minus unknown.

[6]There are 7 patients with unknown/missing classification (4 case and 3 controls). Percentages based on total minus unknown.

[7]There are 7 patients with unknown classification (3 cases and 4 controls). Percentages based on total minus unknown.

[8]There are 6 patients with unknown classification (2 cases and 4 controls). Percentages based on total minus unknown.

Table 3

Management and Outcomes of Military Personnel with and without Tibia Osteomyelitis, No. (%)

	Total (N=215)	Osteomyelitis Cases (N=130)	Controls (N=85)	P-value
First orthopaedic hardware[1]				1.000
External fixation of tibia/fibula	129 (90.8)	74 (91.4)	55 (90.2)	
Internal fixation of tibia/fibula	13 (9.2)	7 (8.6)	6 (9.8)	
Last orthopaedic hardware[1]				<0.001
External fixation of tibia/fibula	75 (52.8)	55 (67.9)	20 (32.8)	
Internal fixation of tibia/fibula	67 (47.2)	26 (32.1)	41 (67.2)	
Any external fixation of tibia/fibula[2]	132 (82.0)	76 (85.4)	56 (77.8)	0.223
Any internal fixation of tibia/fibula[2]	73 (45.3)	31 (34.8)	42 (58.3)	0.004
Time to definitive orthopaedic surgery[1]				0.002
Final stabilization <30 days	66 (46.5)	27 (33.3)	39 (63.9)	
Final stabilization 30 to <60 days	8 (5.6)	6 (7.4)	2 (3.3)	
Final stabilization 2 – 6 months	14 (9.9)	12 (14.8)	2 (3.3)	
Final stabilization >6 months	54 (38.0)	36 (44.4)	18 (29.5)	
Median time to radiographic union (IQR)[3]	191 (121–281)	210 (145–318)	165 (108–229)	0.014
Time to radiographic union[3]				0.282
<6 months	51 (46.8)	22 (38.6)	29 (55.8)	
6 to <9 months	29 (26.6)	16 (28.1)	13 (25.0)	
9 to <12 months	14 (12.8)	9 (15.8)	5 (9.6)	
≥12 months	15 (13.8)	10 (17.5)	5 (9.6)	
Type of foreign body at bone site[4]				0.107
Fragment with hardware	74 (34.6)	50 (38.8)	24 (28.2)	
Fragment only	31 (14.5)	22 (17.1)	9 (10.6)	
Hardware only	76 (35.5)	39 (30.2)	37 (43.5)	
No foreign body	33 (15.4)	18 (14.0)	15 (17.6)	
Bone graft[5]				0.144
Allograft only	6 (2.8)	4 (3.1)	2 (2.4)	
BMP only	19 (8.9)	12 (9.3)	7 (8.3)	
Autograft	2 (0.9)	0	2 (2.4)	
Combination	9 (4.2)	4 (3.1)	5 (6.0)	
Unspecified graft	6 (2.8)	6 (4.7)	0	
Antibiotic beads used[6]	101 (48.1)	77 (59.2)	24 (30.0)	<0.001
Vancomycin	83 (39.5)	63 (48.5)	20 (25.0)	
Death	1 (0.5)	0	1 (1.2)	0.395

BMP - bone morphogenetic proteins; IQR - interquartile range

[1]Excludes patients with transtibial amputations and no type of fixation/hardware (total = 142; osteomyelitis cases = 81; controls = 61)

[2]Excludes patients with transtibial amputations (total = 161; osteomyelitis cases = 89; controls = 72).

[3]Excludes patients with transtibial amputations and missing time to radiographic union (total = 109; osteomyelitis cases = 57; controls = 52)

[4]Foreign body information missing for 1 osteomyelitis case

[5]Bone graft information unknown for 1 osteomyelitis case and 1 control. Percentages based on total minus unknown.

[6]Antibiotic bead use information unknown for 5 controls. Percentages based on total minus unknown. Antibiotic beads were prior to infection diagnosis.

Table 4

Unadjusted Logistic Regression Analysis of Risk Factors Associated with Osteomyelitis in Wounded Military Personnel with Open Tibia Fractures

	Full Population		Restricted Population:Excludes TTAs[1]	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
History of tobacco use	1.52 (0.87–2.68)	0.143	1.32 (0.70–2.50)	0.396
Time period				
2003–2006	1.40 (0.80–2.44)	0.233	1.84 (0.96–3.51)	0.066
2007–2009	Reference		Reference	
Blast mechanism of injury	2.81 (1.50–5.27)	0.001	2.63 (1.32–5.25)	0.006
Blood product transfusions within first 24 hours				
None or missing units	Reference		Reference	
1–9 units	1.90 (1.00–3.63)	0.051	1.46 (0.72–2.97)	0.297
≥10 units	2.01 (0.96–4.21)	0.063	1.49 (0.58–3.79)	0.404
Injury severity score				
0–9 (mild)	Reference		Reference	
10–15 (moderate)	1.31 (0.69–2.50)	0.409	1.19 (0.59–2.41)	0.625
≥16 (severe to life-threatening)	0.90 (0.45–1.81)	0.771	0.72 (0.31–1.65)	0.432
Fracture Class[2]				
GA-II	Reference		Reference	
GA-IIIa	3.63 (1.19–11.06)	0.024	3.63 (1.19–11.06)	0.024
GA-IIIb	8.99 (1.19–11.06)	<0.001	8.99 (2.78–29.00)	<0.001
GA-IIIc	4.91 (1.32–18.20)	0.017	4.91 (1.32–18.20)	0.017
TTA	10.72 (3.31–34.76)	<0.001	NA	
OTA OFC: Skin				
Can be approximated	Reference		Reference	
Cannot be approximated	3.52 (1.68–7.39)	0.001	3.52 (1.68–7.39)	<0.001
Extensive degloving	4.48 (2.11–9.55)	<0.001	4.62 (1.76–12.15)	0.002
OTA OFC: Muscle[3]				
Grade I	Reference		Reference	
Grade II	7.79 (3.20–18.96)	<0.001	7.79 (3.20–18.96)	<0.001
Grade III	9.64 (3.92–23.74)	<0.001	9.35 (2.99–29.26)	<0.001
OTA OFC: Arterial				
No injury	Reference		Reference	
Injury without ischemia	1.92 (0.48–7.75)	0.358	2.00 (0.50–8.09)	0.329
Injury with distal ischemia	1.95 (1.04–3.68)	0.039	1.43 (0.49–4.17)	0.510
OTA OFC: Bone loss				
None	Reference		Reference	
Bone missing/devascularized with contact by proximal/distal fragments	2.30 (1.12–4.75)	0.024	2.46 (1.18–5.14)	0.017
Segmental bone loss	3.69 (1.80–7.57)	<0.001	3.81 (1.52–9.53)	0.004
OTA OFA: Contamination				

	Full Population		Restricted Population:Excludes TTAs[1]	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
None, minimal, or surface	Reference		Reference	
Embedded in bone / deep soft-tissue	3.90 (1.83–8.31)	<0.001	3.87 (1.70–8.83)	0.001
High-risk environmental conditions	2.83 (1.28–6.26)	0.010	2.49 (1.07–5.79)	0.035
Time to definitive orthopaedic surgery[4]	1.00 (1.00–1.00)	0.588	1.00 (1.00–1.00)	0.413
Use of antibiotic beads	3.39 (1.87–6.13)	<0.001	3.54 (1.81–6.93)	<0.001
Type of foreign body at tibia site				
No foreign body	Reference		Reference	
Fragment with hardware	1.74 (0.75–4.02)	0.198	4.00 (0.92–17.39)	0.065
Fragment only	2.04 (0.72–5.73)	0.178	2.00 (0.31–12.84)	0.465
Hardware only	0.88 (0.39–1.99)	0.757	1.78 (0.41–7.71)	0.438
Bone graft				
None	Reference		Reference	
Allograft only	1.32 (0.24–7.41)	0.752	1.75 (0.31–9.90)	0.529
BMP only	1.13 (0.42–3.02)	0.805	1.50 (0.55–4.07)	0.429
Autograft	<0.01 (<0.01 - >999.99)	0.987	<0.01 (<0.01 - >999.99)	0.987
Combination	0.53 (0.14–2.04)	0.354	0.70 (0.18–2.73)	0.606
Unspecified graft	>999.99 (<0.01 - >999.99)	0.978	>999.99 (<0.01 - >999.99)	0.978

CI – confidence interval; GA – Gustilo-Anderson; OR – odds ratio; OTA OFC – Orthopaedic Trauma Association's Open Fracture Classification TTA – transtibial amputation

[1]Analysis excludes TTAs (population: 89 osteomyelitis cases and 72 controls)

[2]Based on a modified GA classification.[28] There were no patients with GA-I fractures in the analysis. TTA were prior to infection.

[3]Grade I - no muscle in area, no appreciable muscle necrosis, some muscle injury with intact function; Grade II - loss of muscle but function remains, some localized necrosis requiring excision, intact muscle-tendon unit; Grade III - dead muscle, loss of function, partial/complete excision, complete disruption of unit, defect does not approximated.

[4]Excludes patients with transtibial amputations and no type of fixation/hardware

Table 5

Adjusted Logistic Regression Analysis of Risk Factors Associated with Osteomyelitis in Wounded Military Personnel with Open Tibia Fractures (Odd Ratios; 95% Confidence Intervals)

Factors	Full Population		Restricted Population:Excludes TTAs[1]	
	GA Class Model[2]	OTA OFC Model[2]	GA Class Model[2]	OTA OFC Model[2]
Time Period				
2003–2006	–	–	4.09 (1.77–9.46)	2.58 (1.05–6.32)
2007–2009	–	–	Reference	Reference
Blast injury mechanism	2.38 (1.14–4.99)	–	3.21 (1.37–7.52)	2.68 (1.06–6.79)
Fracture classification[3]				
GA-II	Reference	–	Reference	–
GA-IIIa	3.06 (0.89–10.54)[4]	–	2.66 (0.75–9.39)[4]	–
GA-IIIb	4.81 (1.33–17.40)	–	5.19 (1.39–19.38)	–
GA-IIIc	5.68 (1.26–25.60)	–	4.08 (0.90–18.50)[4]	–
TTA	15.10 (3.22–71.07)	–	NA	–
Use of antibiotic beads	3.07 (1.59–5.94)	2.86 (1.44–5.69)	4.12 (1.86–9.11)	3.19 (1.33–7.66)
OTA OFC: Muscle,[5]				
Grade I	–	Reference	–	Reference
Grade II	–	5.62 (2.21–14.25)	–	3.99 (1.50–10.59)
Grade III	–	8.46 (3.31–21.64)	–	8.08 (2.16–30.20)
Type of foreign body at tibia site				
No foreign body	Reference	–	–	–
Fragment with hardware	5.65 (1.36–23.38)	–	–	–
Fragment only	4.04 (1.15–14.21)	–	–	–
Hardware only	3.14 (0.83–11.90)[4]	–	–	–

TTA – transtibial amputation; GA – Gustilo-Anderson; OTA OFC – Orthopaedic Trauma Association's Open Fracture Classification

[1]Analysis excludes TTAs (population: 89 osteomyelitis cases and 72 controls)

[2]GA fracture classification and the OTA OFC variables were highly correlated. The multivariable analysis was run separately after selecting for either the GA fracture classification (GA Class Model) or OTA OFC (OTA OFC Model) to be assessed in the model. Stepwise, backward, and forward model selections were conducted to choose the final multivariable risk factor model.

[3]Using a modified GA classification of open fractures.[28] There were no GA-I fractures. TTAs were prior to infection.

[4]P-values for variables that were not significant in the model of the full population are: 0.077 for GA-IIIa and 0.092 for hardware. P-values for variables that were not significant in the model of the restricted population are: 0.129 for GA-IIIa and 0.069 for GA-IIIc.

[5]Grade I - no muscle in area, no appreciable muscle necrosis, some muscle injury with intact function; Grade II - loss of muscle but function remains, some localized necrosis requiring excision, intact muscle-tendon unit; Grade III - dead muscle, loss of function, partial/complete excision, complete disruption of unit, defect does not approximated.