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Deep infections after low-velocity ballistic tibia fractures are frequently polymicrobial and recalcitrant

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Abstract

Objectives: To identify risk factors for developing a fracture-related infection in operatively treated ballistic tibia fractures and to report the microbiologic results of intraoperative cultures.

Design: Retrospective review.

Setting: Level 1 trauma center.

Patients/Participants: One hundred thirty-three adults with operatively treated low-velocity ballistic tibia fractures, from 2011 to 2021.

Intervention: One dose of prophylactic cefazolin or equivalent as well as perioperative prophylaxis.

Main Outcome Measurements: Deep infection rate.

Results: The deep infection rate was 12% (16/134) with no significant difference in injury characteristics, index surgical characteristics, or time to antibiotics between the groups ($P > 0.05$). Patients who were slightly older (35.5 vs. 27 median years, $P = 0.005$) and with higher median body mass indexes (BMIs) (30.09 vs. 24.51, $P = 0.021$) developed a deep infection. 56.3% of patients presented with signs of infection within the first 100 days after injury. Nine patients had polymicrobial infections. There were 29 isolated organisms, 69% were uncovered by first-generation cephalosporin prophylaxis (anaerobes, gram-negative rods, *Enterococcus, methicillin resistant Staphylococcus Aureus [MRSA]*), and 50% of patients developed recalcitrant infection and required a second reoperation where 6 organisms were isolated, half of which were not covered by first-generation prophylaxis (*Enterococcus, Staphylococcus Aureus MRSA*).

Conclusions: We found a deep infection rate of 12% among ballistic tibia fractures receiving standard-of-care antibiotic prophylaxis. Increased age and body mass index were associated with deep infections. Half became recalcitrant requiring a second reoperation. 66.7% of isolated organisms were not covered by first-generation cephalosporin prophylaxis. Consideration should be given to treatment options such as broader prophylaxis or local antibiotic treatment.

Level of Evidence: IV.

Key Words: ballistic, tibia fractures, infections

1. Introduction

With an incidence ranging from 2 to 14%, infections in ballistic fractures are an increasingly common complication encountered by orthopaedic surgeons.[1–4] Amidst a debate around the need for antibiotic prophylaxis and surgical debridement, Prather et al[2] demonstrated that low-velocity ballistic tibia fractures have similar number of operations, nonunion, and infections compared with open tibia fractures. However, there is limited

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information on the clinical course or surgical treatment of infections after ballistic injuries. There is even less information on the microbiome of these infections with most studies investigating combat/high-velocity injuries or unclear criteria differentiating between superficial or deep infection.

Traditionally, most institutions approach prophylaxis in ballistic fractures as an extension of their protocol for open fractures and administer a 1-time dose of cefazolin (or equivalent) in the emergency department in addition to perioperative antibiotics. The purpose of our study was to undertake a retrospective review of low-velocity ballistic tibia fractures and 1) describe risk factors of deep infection and 2) describe the course and surgical management of deep infections.

2. Materials and Methods

Following institutional review board approval, we queried the Trauma Registry from a single Level 1 trauma center to identify all ballistic tibia fractures (OTA/AO 41, 42, 43) treated over a 10-year period from 2011 to 2021.[5] Inclusion criteria were operative tibia fractures caused by low-velocity civilian gunshots. Low velocity was defined as guns with a muzzle velocity of <600 meters/s (ex. 9 mm handgun, 0.45 pistol). For the purpose of this study, we used the consensus definition of fracture-related infection given by Metsemaker et al,[6] which includes both confirmatory and suggestive criteria. We chose to only include patients who met surgical confirmatory criteria with positive intraoperative cultures.[6] We used the consensus definition as studies have directly compared it with the Centers for Disease Control (CDC) surgical site infection criteria and determined that the consensus definition captured 98.9% of fracture-related infections versus <50% for the CDC definition.[7]

Exclusion criteria included skeletal immaturity, age younger than 18 years, fractures caused by high-velocity firearms or shotguns (based on consult note or x-rays), presence of pathologic lesions, prior fracture, or retained implant of the affected bone, or patient death before commencement of treatment. We excluded high-velocity injuries due to their different mechanisms of soft-tissue, thermal injury, and fracture patterns, which are believed to increase the risk of infection when compared with low-velocity injuries.[8]

Per institutional protocol, ballistic fractures received a first-generation cephalosporin on presentation to either the transferring or treating hospital. Ballistic wounds were left open with no closure unless hemostasis was unable to be achieved, in which case, they were loosely closed. All patients who underwent surgical treatment received antibiotics for 24 hours postoperatively. Patients with a documented cephalosporin allergy received vancomycin or clindamycin. All fractures were managed at the time of index presentation by a board-certified orthopaedic surgeon with practice experience in a level 1 trauma center. The majority of surgeons were trauma subspecialty trained. However, after the time of primary fixation, all patients with complications were managed by orthopaedic traumatologists.

All suspected infections were cultured at the time of initial and any subsequent operative debridement.

Collected variables included patient demographics, Charlson Comorbidity Index (CCI), employment history, substance use history, injury characteristics including OTA/AO classification, degree of contamination, bone loss, presence of vascular injury with or without distal ischemia, and wound characteristics, and any ballistic wound debridement or wound closure performed as described by the treating surgeon in the operative report.[5,9] Total length of antibiotic administration and any antibiotic complications were also collected. Regarding microbiology, all intraoperative cultures were reviewed for organisms and antibiotic sensitivities. Complications collected included additional emergency department visits or admissions, nonunion, malunion, implant failure, fracture-related infection, and unplanned additional surgeries.

Statistical analysis was performed by a statistician using SAS software. Categorical variables were compared by χ^2 or Fisher exact test. Parametric continuous variables were compared by Student t test or ANOVA and nonparametric continuous variables by Mann–Whitney U or Kruskal–Wallis test. Significance was defined as *P*-value <0.05 or odds ratio (OR) with confidence interval not overlapping 1.

3. Results

One hundred thirty-three low-velocity operative ballistic tibia fractures were identified (16.5% OTA/AO 41, 69.2% OTA/AO 42, 13.5% OTA/AO 43) (Table 1). Overall, there was a 20.3% infection rate including 11 superficial (8.3%) managed by antibiotics alone and 16 culture-positive deep (12.0%) infections. Two patients were taken to the OR for clinical signs suggesting suspected deep infection or infected nonunion yet yielded negative culture results and were, therefore, not included in the deep infection cohort. One patient initially had a negative culture on their first reoperation but returned to the operating room for a second debridement surgery that yielded positive culture reports and was included in our deep infection cohort.

3.1. Risk Factors

The median age was 27 years (range 22–33) in the noninfected group and 35.5 years (range 30.5–40.5) in the deep infection cohort ($P = 0.005$) (Table 1). The median body mass index (BMI) in the noninfected group (24.51) was less than the median BMI in the infected group (30.09) ($P = 0.021$) (Table 2). Otherwise, there were no identifiable patient risk factors of deep infection between the 2 groups. Overall, most injuries were Gustilo type I/II (89.5%). In the deep infection cohort, there were 14 Gustilo type 1 or 2 fractures and 2 Gustilo type 3 fractures. Other injury characteristics such as arterial injury, bone loss, and need for muscle debridement were compared between the 2 groups, and there was no significant association between the 2 (Table 1). Overall patient outcomes were compared between the 2 cohorts, and we found a statistically significant increase in the number of nonunion/malunion in the infected group (37.5% vs. 7.69%) ($P = 0.003$) as well as more reoperations (100% vs. 5.13%) and readmissions (81.25% vs. 5.13%) ($P < 0.001$).

3.2. Index Management

The average follow-up duration in the deep infection group was 398.6 days (range 153–890) from index surgery. All received 1 dose of cefazolin prophylaxis in the emergency department in addition to preoperative prophylaxis. Time to antibiotics was examined between the 2 groups with no significant differences found (2.78 vs. 2.31 hours, $P > 0.05$) (Table 1). Average number of days to definitive fixation was 0.75 days in the deep infection cohort and 1.68 days in the noninfected ($P = 0.06$). Index operative intervention in this group included plating,[2] intramedullary nailing,[10] and definitive external fixation.[1] Index operation in the group without deep infection was primarily intramedullary nailing (80.1%), plate/screw constructs (14.2%), and, finally,

TABLE 1.

Injury Characteristics

	Without Deep Infections (N = 117)	With Culture-Confirmed Infections (N = 16)	P
OTA/AO classification			
41	19 (16.2)	3 (18.75)	0.802
42	80 (68.4)	12 (75)	
43	17 (14.5)	1 (6.25)	
Gustilo			
Grade 1 and 2	105 (89.7)	14 ()	0.770
Grade 3	12 (10.3)	2 ()	
Skin			
Can be approximated	101 (86.32)	15 (93.75)	>0.999
Cannot be approximated	16 (13.67)	1 (6.25)	
Muscle			
Muscle debridement	48 (41.03)	10 (62.5)	0.219
No muscle debridement required	69 (58.97)	6 (37.5)	
Ballistic wounds I + D'd during surgery			
No	36 (30.77)	3 (7.69)	0.394
Yes	81 (69.23)	13 (81.25)	
Contamination			
Imbedded or high-risk environment	2 (1.71)	0 (0)	0.205
None or minimal contamination	82 (70.09)	8 (50)	
Surface contamination	33 (28.21)	8 (50)	
Bone loss			
Bone missing or devascularized	28 (23.93)	4 (25)	0.074
None	86 (73.5)	10 (62.5)	
Segmental bone loss	3 (2.56)	2 (12.5)	
Length of prophylactic antibiotics			
Less than 24 h	46 (39.32)	1 (6.25)	>0.999
24 h or more	71 (60.68)	15 (93.75)	

TABLE 2.

Demographics

	Without Deep Infections (N = 117)	With Culture-Confirmed Infections (N = 16)	P
Age: median (95% CI)	27 (22, 33)	35.5 (30.5, 40.5)	**0.005**
Gender identity (#)			
F	12 (10.26)	1 (6.25)	>0.999
M	105 (89.74)	15 (93.75)	
BMI: median (95% CI)	24.51 (21.83, 28.57)	30.09 (23.94, 32.88)	**0.021**
Depression			
No	110 (94.02)	16 (100)	0.598
Yes	7 (5.98)	0 (0)	
Smoking			
Current	85 (72.65)	12 (75)	>0.999
Former/never	32 (27.35)	4 (25)	
Smoking type			
Nicotine	79 (91.86)	12 (100)	>0.999
Vaping	4 (4.65)	0 (0)	
Other	3 (3.49)	0 (0)	
Substance misuse/abuse			
No	84 (71.79)	14 (87.5)	0.236
Yes	33 (28.21)	2 (12.5)	
Race			
White	22 (20.37)	3 (18.75)	>0.999
Minority	86 (79.63)	13 (81.25)	
Insurance			
Private/workers' comp	19 (16.24)	7 (43.75)	**0.028**
Public	28 (23.93)	4 (25)	
Self-pay	70 (59.83)	5 (31.25)	
Employment			
Employed/student	63 (64.29)	9 (60)	0.778
Unemployed	35 (35.71)	6 (40)	
Charlson Comorbidity Index			
0	100 (85.47)	12 (75)	0.282
>1	17 (14.53)	4 (24)	

Bold entries signify statistically significant findings at $P < 0.05$.

external fixation. Most of the patients underwent some form of documented soft-tissue debridement of ballistic wounds at the time of fixation (81.3% in the deep infection cohort vs. 69.23% in the non–deep infection cohort, $P = 0.394$).

3.3. Surgical Management of Infection

Of 16 tibias, 9 presented early with signs of infection and underwent reoperation within the first 100 days after initial surgery (mean 58 days, range 10–97). Of these, 6 were treated solely by irrigation and debridement, 2 underwent hardware exchange, and 1 underwent circular fixator placement.[11,12] An additional 7 patients had delayed presentation and underwent reoperation >100 days after initial surgery (mean time 214 days, range 105–521). Five of those patients underwent hardware exchange, and 2 underwent hardware removal. Eight patients required PICC (peripherally inserted central catheter) line placement, and infectious disease was consulted on all patient-s–for management of both inpatient and outpatient antibiotic selection. Patients followed up with both orthopaedics and infectious disease until their treatment course was finished.

3.4. Surgical Management of Recalcitrant Infection

Eight patients (50%) underwent a second reoperation for surgical debridement. Half were patients who initially presented early with infection (mean 110 days, range 24–212), and half had delayed presentation (mean 278 days, range 120–674 days). Five were managed by removal of the intramedullary implant placed at index surgery. Two injuries already united only underwent hardware removal while the other 3 had placement of an antibiotic-coated nail. One of those went on to require a third reoperation where the antibiotic-coated nail was replaced with an antibiotic cement nail. Two patients who already had a removal of hardware at the first reoperation were treated with saucer-ization and one of those had an antibiotic nail placed. Of those 8 patients, 2 went on to require a third reoperation, both of which was a repeat exchange nail procedure.

3.5. Isolated Organisms

At the first debridement surgery, a total of 29 bacterial organisms were isolated. Nine of the 16 (56.3%) patients had polymicrobial infections, 5 of which became recalcitrant. The most common organisms isolated at first reoperation were gram negatives and gram positives not susceptible to first-generation prophylaxis (69%) (methicillin-resistant *Staphylococcus aureus* (MRSA) (24.1%), gram-negative rods and anaerobes at 17.2% each, and Enterococci (10.3%)). Gram positives susceptible to first-generation prophylaxis made up 31% of isolated organisms (methicillin-sensitive *S. aureus*, *Streptococci* (20.7%), and gram-positive rods and *Escherichia coli* at 3.4%) (Fig. 1).

In the 8 patients with recalcitrant infections requiring a second operation, there were a total of 6 organisms isolated. Of the 6 organisms isolated, 3 were uncovered by first-generation cephalosporins (50%) (Fig. 2). One patient was polymicrobial on both first and second debridement cultures and went on to require a third reoperation. In both sets of cultures, he was positive for *Enterococcus* until his third surgery, at which point his culture was negative.

Two patients who were polymicrobial at their first reoperation went to require a third reoperation—one yielded negative cultures and the other continued to grow gram-negative rods.

4. Discussion

The purpose of this study was to identify risk factors and describe the treatment course and management of low-velocity ballistic tibia fractures that met the surgical confirmatory criteria of the consensus definition of fracture-related infection by Metsemaker et al.[10,13,14] Overall, we found an 8.3% superficial infection rate and 12.0% deep infection rate. These deep infections required further intervention and were associated with a higher rate of nonunion (37.5% vs. 9%), reoperation (100% vs. 5.13%), and readmission (81.25% vs. 5.13%) ($P < 0.001$). Our findings are similar to a study by Lee et al[4] who reviewed 121 ballistic tibias and found an overall 14% deep infection rate and 20% nonunion rate.

Despite these high complication rates, management of ballistic tibias is controversial, with most institutions lacking any sort of formalized protocol.[15,16] One of these areas of debate is the need for surgical debridement of ballistic wounds. In our study, we found no significant difference in the incidence of deep infection between those who received debridement of the ballistic wounds at the time of operative fixation ($P = 0.394$).

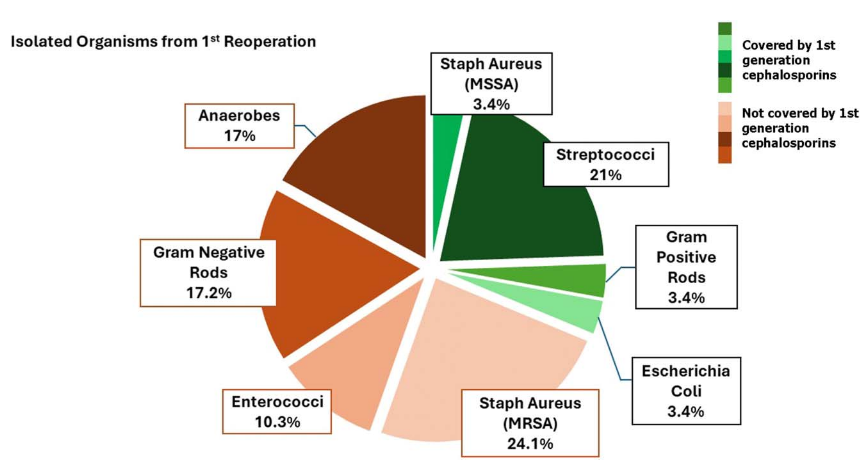

Figure 1. Isolated organisms from first reoperation.

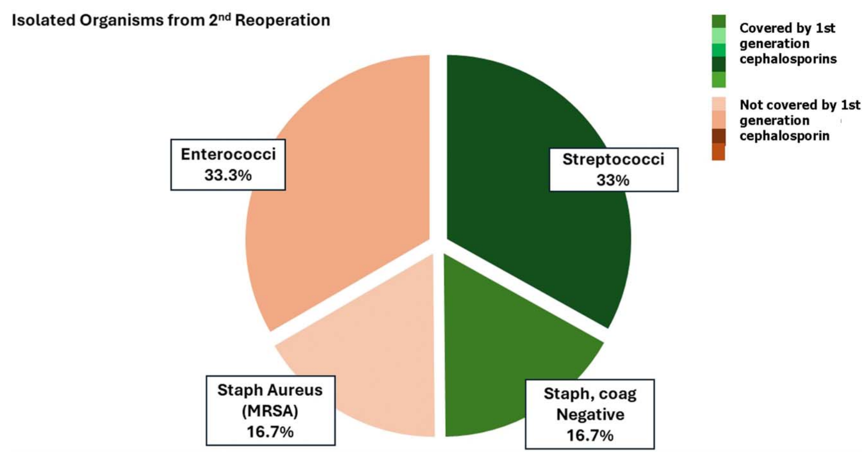

Figure 2. Isolated organisms from second reoperation.

With the high deep infection rate in our cohort (11.9%), we took a closer look at the 16 tibias that required reoperation for infection. We found that patients with deep infection were older (35.5 years vs. 27 years, $P = 0.005$) and had a higher BMI (30.1 vs. 24.5, $P = 0.021$) A slight majority (56%) of these infections were diagnosed within 100 days from index surgery and treated with irrigation and debridement with either retention of hardware or exchange hardware exchange. In our cohort, we had a high rate (50%) of recalcitrant infection requiring a second reoperation, half of which initially presented early with infection and half had delayed presentation. In regard to predictive factors for recalcitrant infection, we were underpowered and unable to make any conclusions regarding the management, including the amount of debridement, hardware exchange, or timing of antibiotic administration or course, in patients who developed recalcitrant infection and those who did not.

Although the efficacy of perioperative prophylaxis is well established following operative fracture, many studies suggest that it is not effective at preventing infection in nonoperative or isolated soft-tissue ballistic injuries.[3,17–20] Despite the inconsistency in the literature regarding antibiotic prophylaxis, a survey conducted of 2015 Orthopaedic Trauma Association surgeons found that 85% of orthopaedic surgeons still prescribe first-generation cephalosporins for prophylaxis.[16] A variety of reasons were cited including personal preference, fear of litigation, and influence of previous training. At our institution, all ballistic fractures received a one-time dose of

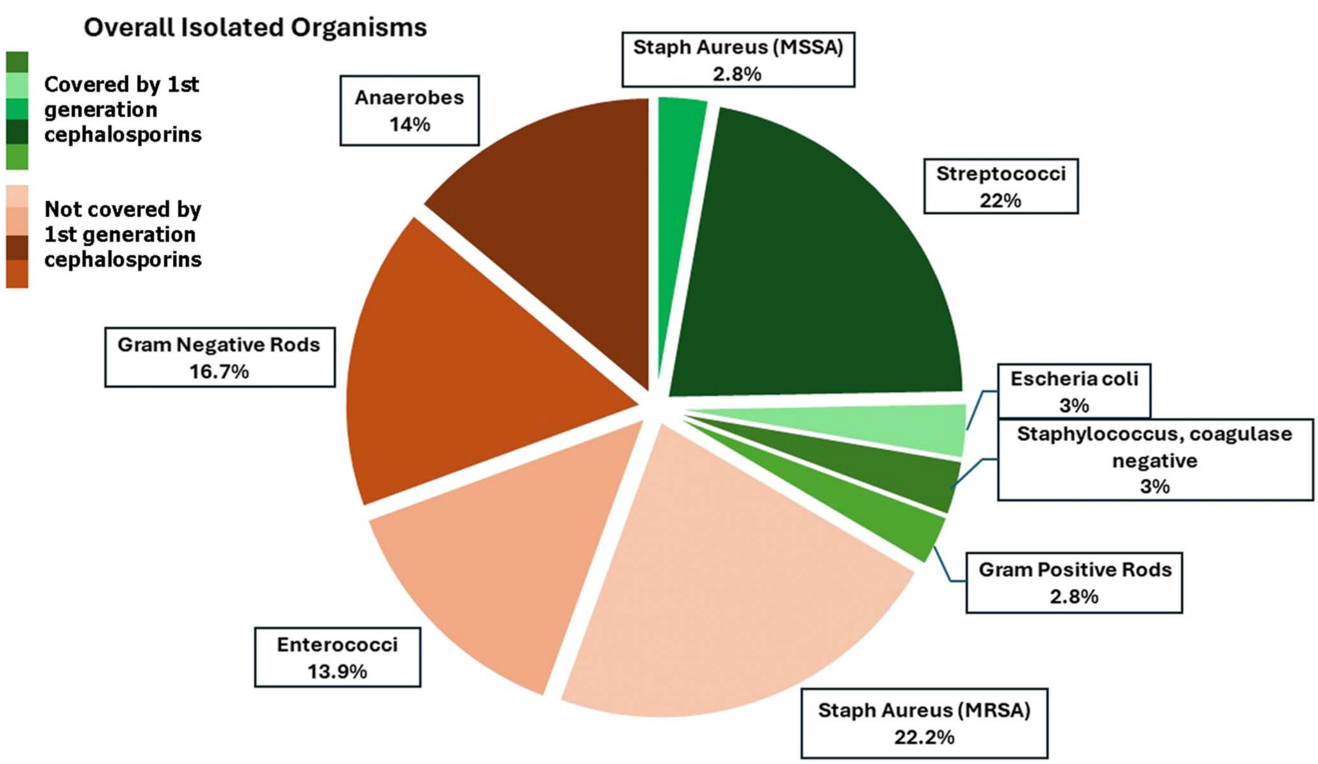

Figure 3. Overall isolated organisms.

cefazolin in the emergency department at the time of presentation; however ,we found no significant difference in time to antibiotics between the 2 cohorts. To evaluate effectiveness of antibiotic prophylaxis, we also looked at intraoperative culture reports. In the literature, there is a significant gap regarding the microbiology observed in postoperative low-energy ballistic fracture-related infections. Some literature has explored cultures from high-velocity penetrating injuries finding isolates of *Staphylococcus Aureus*, gram-negative rods, and *Streptococci*.[8] However, high-velocity injuries are influenced by a wide variety of other factors given their difference in injury burden, thermal injury pattern, and gross contamination, thus limiting the application of these studies.[8] Our study adds to the limited literature on this topic. Overall, 50% (n = 8) of infections were polymicrobial and 62.5% (n = 5) developed recalcitrant infection requiring a second reoperation. Among all cultures, we found 36 isolated organisms, 66.7% of which were not covered by first-generation cephalosporins, the backbone of current antibiotic prophylaxis for open fractures (Fig. 3). Looking specifically at the 29 isolated organisms at the first reoperation, the most common isolate was *Staphylococcus Aureus* MRSA (24.1%) and Streptococci (20.7%) (Fig. 1). This is similar to the study by Nguyen et al,[17] which reported that *Staphylococcus Aureus* and *Streptococcus* as reported isolates. However, what was surprising was the relatively high prevalence of gram-negative rods and anaerobes (17.2% each). Of the patients with recalcitrant infection, there were 6 isolated organisms, 50% of which were minimally covered by first-generation prophylaxis.

There are several limitations to note. First, the study is retrospective and we have a relatively small cohort of 16 patients, limiting our ability to make a broad conclusion and recommendations regarding antibiotic prophylaxis and surgical management. Second, there is the possibility that the rate of infection could be higher than what we identified. Average follow-up duration in our infection cohort was 398.6 days; however, there is the possibility that patients could have sought further treatment at another facility. Finally, this is a small descriptive case series over a long period (10 years) with high surgeon variance in both extent of debridement and clinical decision making. There was no standardized definition of what entailed "operative debridement" outside the operative documentation, which could lead to variance in what each surgeon determined to be adequate debridement at the time of fixation.

Areas for future study would include a randomized controlled trial exploring the role of local antibiotics during index management of these injuries as well as possibly expanding antibiotic prophylaxis to cover gram negatives and anaerobes similar to Gustilo Type III injuries.[21]

In conclusion, we found that age and BMI were nonmodifiable patient risk factors associated with deep infections of ballistic tibia fractures. These patients also had a higher rate of nonunion, reoperation, and readmission. We found that these deep infections were often polymicrobial and recalcitrant. These findings should be considered by the treatment team when managing infections and complications of low-velocity ballistic fractures.

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