

# Classification and Incidence of Bacterial Infections and Risk Factors for Recurrent Osteomyelitis in Infected Nonunion and Osteomyelitis Patients After Bone Fracture



Samuel Merrill, BS; Nicole Griffin, MS; Hunter LaCouture, BS;  
Johnathan Layne, BS; Mohamad Awad, MD, MBA; Jason W. Stoneback, MD



## Introduction

Osteomyelitis is a complex clinical problem with a high recurrence rate<sup>1</sup> that can occur due to reinfection of the original organism or with a different pathogen<sup>3</sup>. Previous studies suggest that gram positive cocci are the most common cause of bone infections<sup>2, 6</sup> and have identified possible risk factors for recurrence: repeated operations, post-traumatic osteomyelitis<sup>5, 7, 10</sup>, internal fixation at first stage bone exposure<sup>9</sup>, and *Pseudomonas aeruginosa* infection<sup>8</sup>. However, the comprehensiveness of these studies is lacking. The purpose of this study is to investigate the most common bacteria in traumatic osteomyelitis and infected nonunion cases and identify risk factors for recurrent osteomyelitis in these patients.

## Methods

A retrospective analysis of 1825 patient charts following fracture fixation with a diagnosis of an infected non-union or osteomyelitis was conducted from 2006-2018. Included patients must have had a CRP, ESR, or CBC measured within 5 days of diagnosis, must have undergone surgical intervention at the University of Colorado Hospital, and had documented follow-up for >1 year, and have complete documentation in their chart including information on past diagnoses and treatment for osteomyelitis.

**Statistical Methods:** We performed a descriptive analysis for both nominal and categorical variables and a multivariate analysis for risk factors for recurrent osteomyelitis, including demographic data, comorbidities, location of osteomyelitis, microbiologic data, and surgical outcome data. Statistical analysis with linear regression was performed using JMP SAS software.

## Results

141 patients were included with a mean age of 53.65 ± 14.8 years old, 69.5% of them being male – **Table 1**. The most common comorbidities were tobacco use (49.6%) and hypertension (49.6%) – **Table 2**. The most common locations of osteomyelitis were tibia/fibula (20.6%) and spine (20.6%). The most common type of bacteria isolated in those patients with infected nonunion were MSSA (42.6%) and MRSA (14.9%) – **Table 3**. The top antibiotics administered were Vancomycin (45.4%), Doxycycline (16.3%), and Daptomycin (14.2%) – **Table 4**. The top complications were wound healing problems (37.5%) and recurrent infection (38.3%) – **Table 5**. Odds of developing recurrent osteomyelitis are shown in **Table 6**. At a p = .05, variables with a statistically significant positive effect on odds of developing recurrent osteomyelitis were days until infection (p = 0.025), elevated hematocrit (p = 0.016), and # of complications (p = 0.013). Elevated hemoglobin (p = 0.021) and elevated CRP (p = 0.0017) both had a negative effect on the odds of developing recurrent osteomyelitis.

**Table 1. Comorbidities for Osteomyelitis**

	n	% of Patients
Male Sex	98	69.5%
Age in Years, Mean (Standard Deviation)	53.65 ± (14.8)	
Race		
- Caucasian	96	68.1%
- Black, African American	16	11.3%
- Asian	0	0%
- Native American	1	0.7%
- Unknown	10	7.1%
Hispanic	13	9.3%
Osteomyelitis	129	91.5%
Infected Non-union	12	8.5%
Co-morbidities		
- Diabetes	21	14.9%
- HbA1C > 7.0	16	11.3%
- Hypertension	70	49.6%
- Immunosuppressive Drugs	11	7.8%
- Tobacco Use (within last year)	70	49.6%
- Marijuana Use	6	4.3%
- Peripheral Vascular Disease	8	5.7%
- Coronary Artery Disease	18	12.8%
- No Co-morbidities	41	29.1%
- Malignancy	10	7.1%
Antibiotics Until Achieving Union	118	90.8%
Blood Culture	15	10.6%
Tissue Culture	137	97.7%
- Non-operative	10	7%
- Operative	127	92.7%
White Blood Cells (WBC)	9.6 g/dL ± (4.5)	
Red Blood Cells (RBC)	4.13 g/dL ± (0.7)	
Hematocrit	36.6 g/dL ± (6.5)	
Hemoglobin	12.1 g/dL ± (2.3)	
Platelet Count	128.8 g/dL ± (299.3)	

**Table 2. Location of Osteomyelitis**

Location	Frequency	%
Tibia/Fibula	31	20.6%
Spine	29	20.6%
Foot	28	19.9%
Ankle	12	8.5%
Femur	9	6.4%
Knee	6	4.3%
Hip	6	4.3%
Hand	5	3.5%
Elbow	4	2.8%
Shoulder	2	1.4%
Wrist	2	1.4%
Humerus	2	0.7%
Radius/Ulna	1	0.7%
Other	35	24.8%

**Table 3. Pathogens Found in Patients Diagnosed with Osteomyelitis**

Bacteria Type	Frequency	%
Actinobacter baumannii	1	0.7
Acinetobacter Lwoffii	0	0
Burkholderia cepacia	0	0
Candida albicans	2	1.4
Enterobacter cloacae	10	7.1
Enterococcus faecalis	19	13.5
E. coli (Escherichia coli)	7	5
Klebsiella pneumoniae	2	1.4
MRSA (Methicillin-resistant Staphylococcus aureus)	21	14.9
MRSE (Methicillin-resistant Staphylococcus epidermidis)	2	1.4
MSSA (Methicillin-sensitive Staphylococcus aureus)	60	42.6
Proteus bacilli	2	1.4
Pseudomonas aeruginosa	8	5.7
Raoultella ornithinolytica	0	0
Raoultella planticola	0	0
Serratia marcescens	2	1.4
Serratia subspecies (other)	1	0.7
Staphylococcus epidermidis	8	5.7
Other	70	49.6

**Table 4. Antibiotics**

Antibiotics Type	Frequency	%
Vancomycin	64	45.4
Cefazolin	17	12.1
Tobramycin	2	1.4
Ampicillin	3	2.1
Sulbactam	1	0.7
Ceftriaxone	20	14.2
Ceftazidime	2	1.4
Meropenem	3	2.1
Piperacillin	6	4.3
Ciprofloxacin	9	6.4
Levofloxacin	13	9.2
Moxifloxacin	2	1.4
Doxycycline	23	16.3
Clindamycin	11	7.8
Metronidazole	16	11.3
Daptomycin	20	14.2
Cefepime	8	5.7
Fosfomycin	0	0
Enoxacin	0	0
Linezolid	0	0
Other	68	

**Table 5. Frequency of Complications**

Complication	Frequency	%
Wound Healing Problem	53	37.6
Recurrent Infection	54	38.3
Urinary Tract Infection	7	5
Venous Thromboembolism	3	2.1
Neuropathy	7	5
Mortality	1	0.7
Other*	16	11.3

\*Other includes wound dehiscence, skin ulcers near surgical site, hardware infection, and amputation.

**Table 6. Modeling the Odds of Recurrent Osteomyelitis**

	Estimate	Std. Error	t-value	p-value
Sex (Male = 1)	-1.730	1.251	-1.383	0.167
Age	-0.087	0.050	-1.735	0.083
Days until Infection	0.001	0.001	2.240	0.025
WBC	-0.312	0.602	-0.518	0.605
RBC	-1.656	1.428	-1.160	0.246
Hemoglobin	-1.805	0.781	-2.310	0.021
Hematocrit	0.657	0.274	2.401	0.016
Platelet Count	-0.006	0.006	-0.907	0.364
Neutrophil Absolute	1.408	0.729	1.932	0.053
Lymphocyte Absolute	0.223	0.510	0.436	0.663
Monocytes Absolute	-4.664	2.500	-1.865	0.062
Eosinophils Absolute	13.747	7.291	1.885	0.059
Basophils Absolute	-5.486	12.828	-0.428	0.669
Immature Granulocytes Absolute	3.116	5.922	0.526	0.599
CRP	-0.064	0.027	-2.384	0.017
ESR	0.006	0.024	0.235	0.814
Abx Regimen Continued (Yes = 1)	2.355	1.914	1.231	0.218
# of I&D	0.149	0.333	0.447	0.655
# Comorbidities	0.831	0.590	1.407	0.159
# Complications	2.403	0.969	2.481	0.013
# Infections	0.111	1.344	0.083	0.934
# Organisms Present	0.355	0.904	0.393	0.695
Infection Location (Axial = 1)	-11.798	2239.907	-0.005	0.996

**Days until Infection:** As days after fracture until diagnosis of infection increases by one unit, the odds of developing recurrent osteomyelitis **increases** by a factor of 1.001.

**Hemoglobin:** A one unit increase **decreased** odds of developing recurrent osteomyelitis by 83.6%.

**Hematocrit:** As hematocrit increases by one unit, the odds of developing recurrent osteomyelitis **increases** by a factor of 1.93.

**CRP:** A one unit increase, **decreased** the odds of developing recurrent osteomyelitis by 6.2%.

**# Complications:** As the number of complications increases by one unit, the odds of developing recurrent osteomyelitis **increases** by a factor of 11.06.

## Limitations

Limiting factors of this study are largely due to strict inclusion criteria. Of the 1,825 charts originally returned by the ICD codes, only 141 met all inclusion criteria. A significant contributing factor was the high number of diabetic foot wounds who went on to develop osteomyelitis without evidence of fracture and were subsequently excluded.

## Conclusions

- Gram positive cocci were the most prevalent causal organisms.
- The most common complications by far were wound healing problems and recurrent infection.
- Factors for increased risk of recurrent osteomyelitis: more days post-fracture until infection, elevated hematocrit, and increased number of complications.
- Factors for decreased risk of recurrent osteomyelitis: elevated hemoglobin and elevated CRP.
- Potential for future streamlined treatment protocol: bug → abx → complications to watch for → risk of recurrence

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**Conflicts of Interest:** No disclosures