

RESEARCH ARTICLE

Implant Removal Due to Infection After Open Reduction and Internal Fixation: Trends and Predictors

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Received: 27 November 2020

Accepted: 25 October 2021

Abstract

Background: Implant removal due to infection is one of the major causes failure following open reduction and internal fixation (ORIF). The aim of this study was to determine trends and predictors of infection-related implant removal following ORIF of extremities using a nationally representative database.

Methods: Nationwide Inpatient Sample data from 2006 to 2017 was used to identify cases of ORIF following upper and lower extremity fractures, as well as cases that underwent infection-related implant removal following ORIF. Multivariate analysis was performed to identify independent predictors of infection-related implant removal, controlling for patient demographics and comorbidities, hospital characteristics, site of fracture, and year.

Results: For all ORIF procedures, the highest rate of implant removal due to infection was the phalanges/hand (5.61%), phalanges/foot (5.08%), and the radius/ulna (4.85%). Implant removal rates due to infection decreased in all fractures except radial/ulnar fractures. Tarsal/metatarsal fractures (odds ratio (OR)=1.45, 95% confidence interval (CI): 1.02-2.05), and tibial fractures (OR=1.82, 95% CI: 1.45-2.28) were identified as independent predictors of infection-related implant removal. Male gender (OR=1.67, 95% CI: 1.49-1.87), Obesity (OR=1.85, 95% CI: 1.34-2.54), diabetes mellitus with chronic complications (OR=1.69, 95% CI: 1.13-2.54, $P<0.05$), deficiency anemia (OR=1.59, 95% CI: 1.14-2.22) were patient factors that were associated with increased infection-related removals. Removal of implant due to infection had a higher total charge associated with the episode of care (mean: \$166,041) than non-infection related implant removal (mean: \$133,110).

Conclusion: Implant removal rates due to infection decreased in all fractures except radial/ulnar fractures. Diabetes, liver disease, and rheumatoid arthritis were important predictors of infection-related implant removal. The study identified some risk factors for implant related infection following ORIF, such as diabetes, obesity, and anemia, that should be studied further to implement strategies to reduce rate of infection following ORIF.

Level of evidence: III

Keywords: Fracture, Implant removal, Infection-related implant removal, Infection, Septic hardware

Introduction

The medial collateral ligament (MCL) injury is the most common injury to the knee accounting for about 40% of knee injuries (1). The incidence of

MCL injuries is 0.24/1000, with a 2:1 male to female ratio (2). In athletes, the incidence increases to 7.3/1000 population (3). The main medial static stabilizers of the

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knee are the superficial MCL, deep MCL, and posterior oblique ligament (POL) (4).

The MCL lies in the second layer in the medial aspect of the knee, the femoral attachment lies 1-mm proximal and 37 mm posterior to the medial femoral epicondyle, the distal bony attachment is located just anterior to the posteromedial crest of the tibia 42–71 mm from the tibial joint line, and the superficial MCL is the main medial static stabilizer of the knee all over the range of motion (4-6).

The deep MCL is a thickening of the joint capsule. It consists of two distinct components: the menisocofemoral ligament is distal and deep to the femoral attachment of the superficial MCL approximately 6-mm distal and 5-mm posterior to the medial epicondyle; the meniscotibial portion, which is shorter and thicker, attaches just distal to the edge of the articular surface of the medial tibial plateau (5,6).

The femoral attachment of the POL extends from the posterosuperior aspect of superficial attachment of MCL to the gastrocnemius tubercle and is divided into three components, superficial, capsular, and most importantly, the central arm (5-7). The central arm arises from the main tendon of the semimembranosus, directly attached to the posterior joint capsule and posterior meniscus, and blends its attachment on the tibia 5-mm below the tibial plateau (5,8). The POL is a valgus stabilizer when the knee is extended and has a role in maintaining rotational stability of the knee, especially in PCL-deficient knees (9).

The incidence of concomitant ligamentous injury with grade 3 MCL injury is about 80%, most of which are associated with anterior cruciate ligament (ACL) injury (10,11).

MCL is known for its good healing potential rather than intracapsular ligaments, so nonoperative treatment is the rule for treatment of MCL injuries in grades 1 and 2 and selected cases of grade 3 injuries (12, 13). Failed nonoperative treatment in grade 3 injuries leads to deterioration in knee function and subsequent osteoarthritis in 63% of cases after 10 years (14).

Several techniques have been described for MCL reconstruction however; no evidence supports one technique over the others (15).

This study aims to describe the minimally invasive reconstruction of the MCL of the knee and to evaluate the functional outcome and medial joint space opening 18 months postoperatively.

Materials and Methods

Data Source

We analyzed data from the Nationwide Inpatient Sample (NIS) from 2006 to 2017 to determine the trend and predicting factors of implant removal due to infection after ORIF. The NIS was chosen because it is the largest longitudinal national database in the United States, capturing 20% of hospitalizations annually. The database contains demographic, medical, and financial information associated with each episode of care from 1,051 hospitals across 15 states, and is maintained by the Healthcare Cost and Utilization project and the Agency for Healthcare Research and Quality(15,16). US population data was obtained from the census.gov

website for each year (2006-2017)(17). This study was exempt from institutional board approval as all data was retrieved from the NIS.

Patient Selection

The NIS was queried from 2006 to 2017 for patients undergoing ORIF or implant removal each year using a method described by Lovald et al(1,18). Patients were identified via the Ninth Revision of the International Classification of Diseases (ICD-9 codes) for ORIF (79.8x) of the following humeral, radial/ulnar, carpal/metacarpal, femoral, tibial/fibula, tarsal/metatarsal fractures(19). Patients who underwent implant removal (78.6x) and those who developed infection following implant implantation (996.66 and 996.67) were identified as well. A total of 924,506 patients underwent ORIF, and 41,071 patients underwent remove of implant during the study period.

Data collection included demographic information (Age, gender, race), and medical comorbidities. Hospital factors including hospital size (small, medium, or large), type (academic urban, private urban, or rural), and financial data (length of stay, and hospital charges) were also collected. Lastly information regarding the implant, including indication for removal (aseptic or septic (ICD-9 code 996.66 and 996.67)), and location of implant were collected. In regards to the medical comorbidities collected, the conditions included in the Charlson Comorbidity Index (CCI) and the Elixhauser Comorbidity Measure (ECM), due to proven validity and common use in evaluating the NIS, and were identified using the ICD-9CM codes(20–22). The conditions included in these two indices are: age, alcohol abuse, drug abuse, liver disease (mild or severe), rheumatological conditions, peripheral vascular disease, chronic pulmonary disease, blood loss anemia, iron deficiency anemia, HIV/AIDS, solid organ tumor, lymphoma, metastatic disease, diabetes (uncomplicated or complicated), hemiplegia/paraplegia, and myocardial infarction.

Outcome Variables

The primary outcome measure of this study was impact of infection on implant removal following ORIF from 2006 to 2017. Additional secondary outcomes of this study were to identify independent predictors of implant removal due to infection, and the impact infection on the length of stay (LOS) and hospital charges in comparison with aseptic removal of implants.

Statistical Analysis

The impact of infection on implant removal on the LOS and hospital charges in comparison to aseptic implant removal was determined using Wilcoxon Rank-Sum Test. The rate of ORIF each year was determined using the NIS and census data. Similarly, the rate of aseptic implant removal and implant removal due to infection each year was determined using the NIS data and the census data to calculate rate per 100,000 of the national population. The removal of implant was further stratified by dividing the number of implant removals in a region of the body by the total number of ORIF procedures performed on that region each year.

The removal of implant due to infection was further stratified by dividing the number of implant removals due to infection in a region of the body by the total number of implant removal procedures performed on that region each year.

Logistic regression analysis was performed, controlling for age, gender, ethnicity, medical comorbidities, hospital type and size, and fracture location to identify independent predictors of implant removal due to infection. Logistic regression was used to estimate the contribution of patient and hospital factors to the probability that a patient visit was for the removal of implant. The regressions included interaction terms between calendar year and site of implant/removal so that statistical comparisons could be made between different bones and the femur (used as reference due to its relatively high rate of fracture).

In order to estimate the incidence on a national population scale, the US population data was obtained from the census.gov, and used in conjunction with the population weight estimates provided by the NIS in order to generate national estimates of the outcomes. The hospital charges were adjusted to 2017 dollars using the inflation calculator provided by the US Bureau of Labor Statistics (23). We used R 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) for all analyses and the 'rms' package within R for the logistic regression. In all analyses, p-values less than 0.05 were statistically significant.

Results

ORIF Procedures

The rate of ORIF procedures were determined through using the NIS database from 2006 to 2017. During the 11-year study period, the overall rate of ORIF decreased from 28.4 to 17.3 per 100,000 (38.9%) [Table 1 and Figure 1]. This decrease was seen in the humerus (2.2 to 1.1 per 100,000, 50.2%), femur (10.6 to 5.8 per 100,000, 45.2%), phalanges/hand (0.43 to 0.24 per 100,000, 44.1%), and tibia/fibula (9.7 to 5.7 per 100,000, 41.3%). The most common location for ORIF was the femur (36.2%), followed by the tibia/fibula (34.0%), and radius/ulna (11.2%).

Trends in Implant Removal

The rate of implant removal across the study period decreased from 1.02 to 0.60 per 100,000 (41.7%). The greatest decrease was seen in the phalanges/foot (-81.6%), humerus (-68.4%), and phalanges/hands (-63.3%) [Figure 2]. The highest rate of implant removal for any reason was removal from the radius/ulna (21.0%), followed by the hands/phalanges (16.5%) and carpal/metacarpal (13.5%).

Trends in Infection-Related Implant Removal

The rate of infection-related implant removal across the study period decreased from 0.039 to 0.025 per 100,000 (41.7%). The greatest decrease was seen in the humerus (-84.7%), tibia/fibula (-63.0%), and tarsal/

Table 1. Predictors of Implant removal due to infection

Predictors of Implant Removal	Odds Ratio	95% CI Lower Limit	95% CI Upper Limit	P-Value
Blood loss anemia	2.94	1.32	6.56	<0.001
Hospital Type - Urban Non-Teaching	2.63	2.22	3.12	<.0001
Psychoses	2.43	1.44	4.13	<0.001
Obesity	1.85	1.34	2.54	<0.001
Fracture Location - Tibia/Fibula	1.82	1.45	2.28	<.0001
Fracture Location - Unspecified	1.72	1.25	2.36	<0.001
Diabetes with chronic complications	1.69	1.13	2.54	<0.05
Sex - Male	1.67	1.49	1.87	<.0001
Age (51-60)	1.67	1.46	1.90	<.0001
Deficiency anemias	1.59	1.14	2.22	<0.01
Depression	1.52	1.07	2.15	<0.05
Age (41-50)	1.50	1.29	1.75	<.0001
Fracture Location -Tarsal/Metatarsal	1.45	1.02	2.05	<0.05
Hospital Size - Small	1.36	1.20	1.55	<.0001
Length of Stay	1.03	1.03	1.03	<.0001
Age (<41)	0.85	0.74	0.97	<0.05
Hospital Size - Medium	0.84	0.72	0.98	<0.05
Age (>70)	0.42	0.36	0.48	<.0001
Hospital Type - Urban Teaching	0.39	0.29	0.53	<.0001

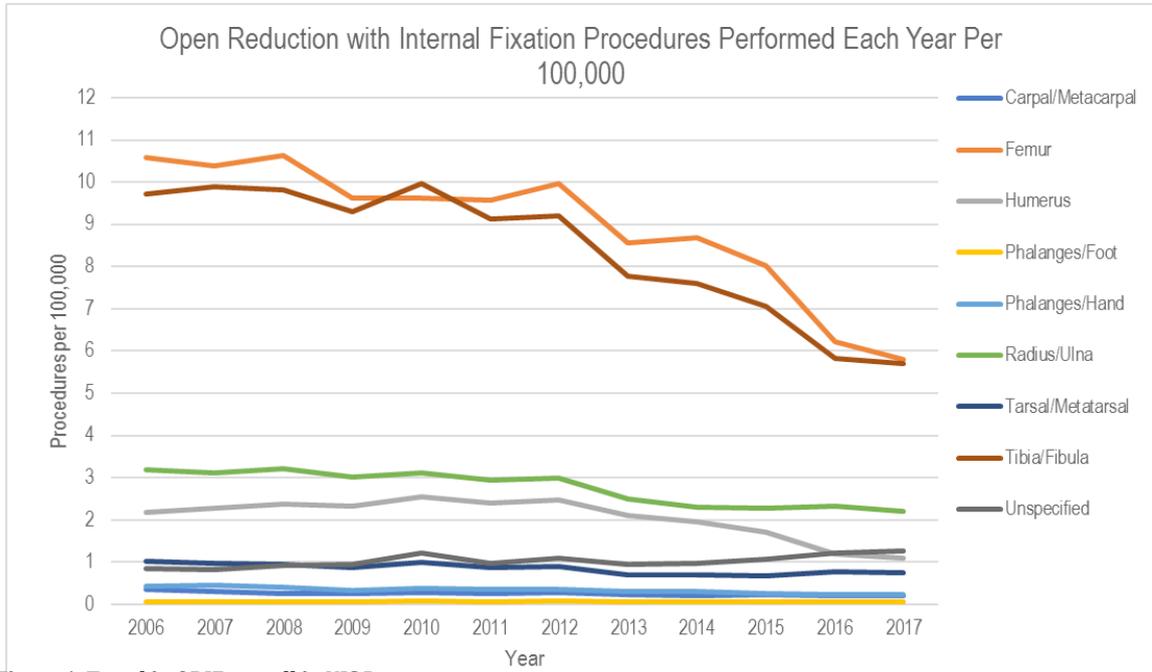


Figure 1. Trend in ORIF overall in NIS Data.

metatarsal (-44.9%) [Figure 3]. There was an increase in the rate of infection-related implant for the radius/ulna (41.9%, 0.0037 to 0.0052). The highest rate of implant

removal due to infection was the phalanges/hand (5.61%), phalanges/foot (5.08%), and the radius/ulna (4.85%) [Figure 4]. The most common implant location

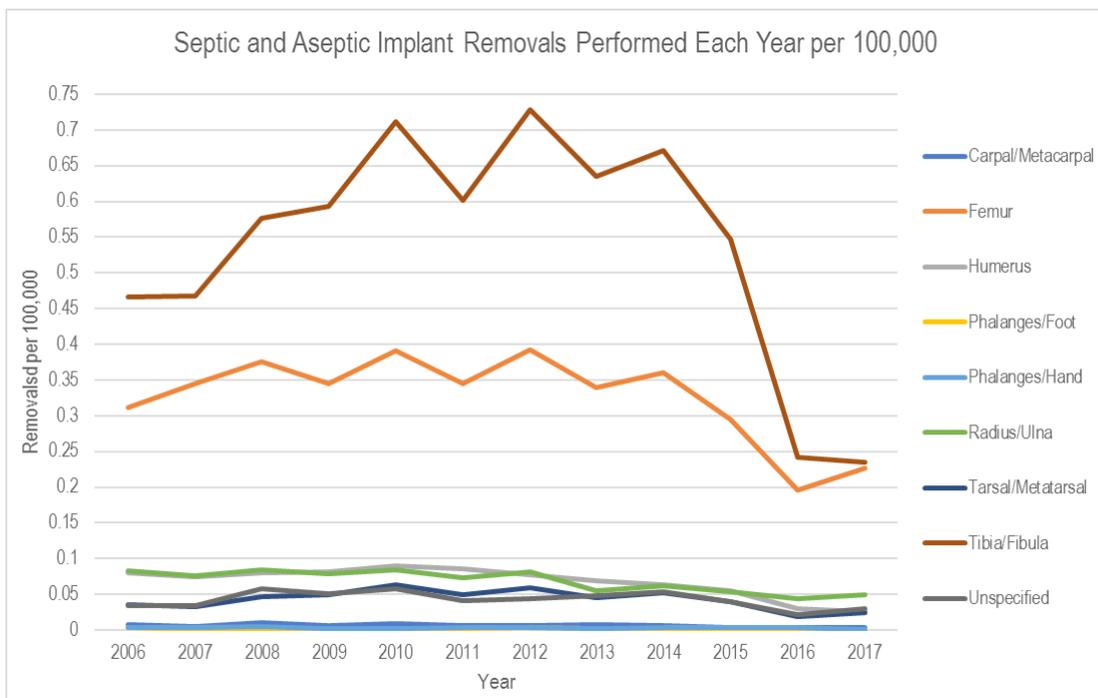


Figure 2. Trend in Implant removal by body region.

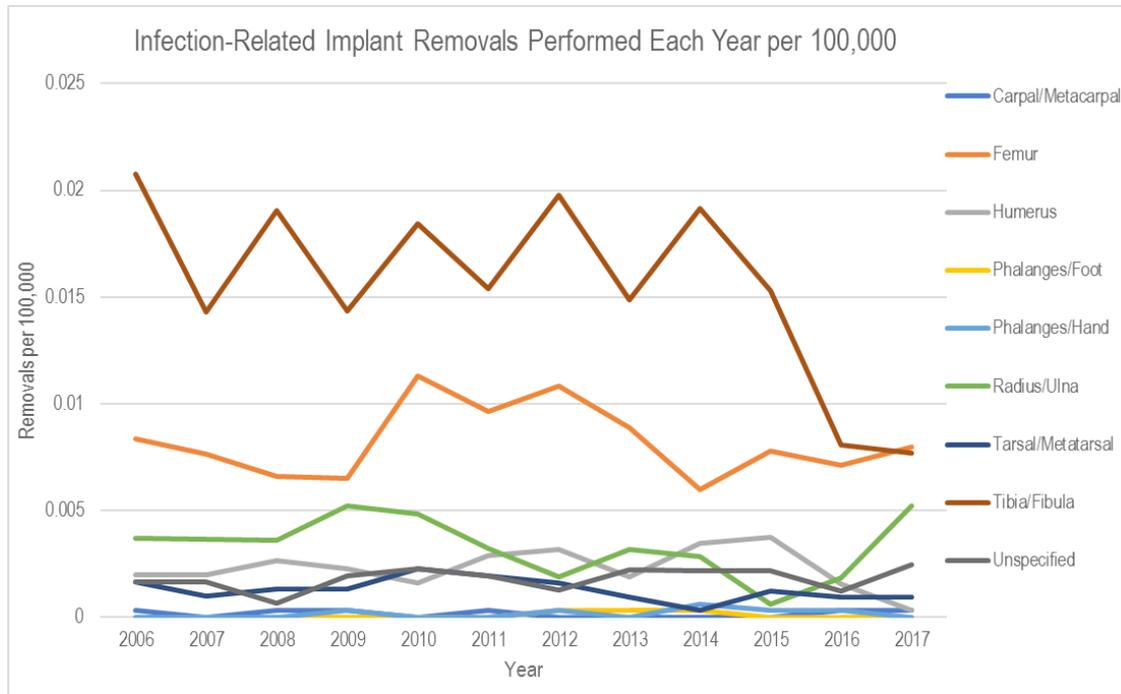


Figure 3. Trend in Implant Removal due to infection by body region.

associated with infection-related implant removal was the phalanges/hand (22.0%) and carpal/metacarpal (22.0%), followed by the humerus (11.0%).

Predictors of Infection-Related Implant Removals

Logistic regression analysis was performed to identify independent predictors of implant removal due to infection [Figure 5]. In terms of body region, tarsal/

metatarsal fractures (odds ratio (OR)=1.45, 95% confidence interval (CI): 1.02-2.05, $P<0.05$), and tibial fractures (OR=1.82, 95% CI: 1.45-2.28, $P<0.001$) were identified as independent predictors of infection-related implant removal. Medical comorbidities determined to be significant predictors included obesity (OR=1.85, 95% CI: 1.34-2.54, $P<0.001$), diabetes mellitus with chronic complications (OR=1.69, 95% CI: 1.13-2.54, $P<0.05$),

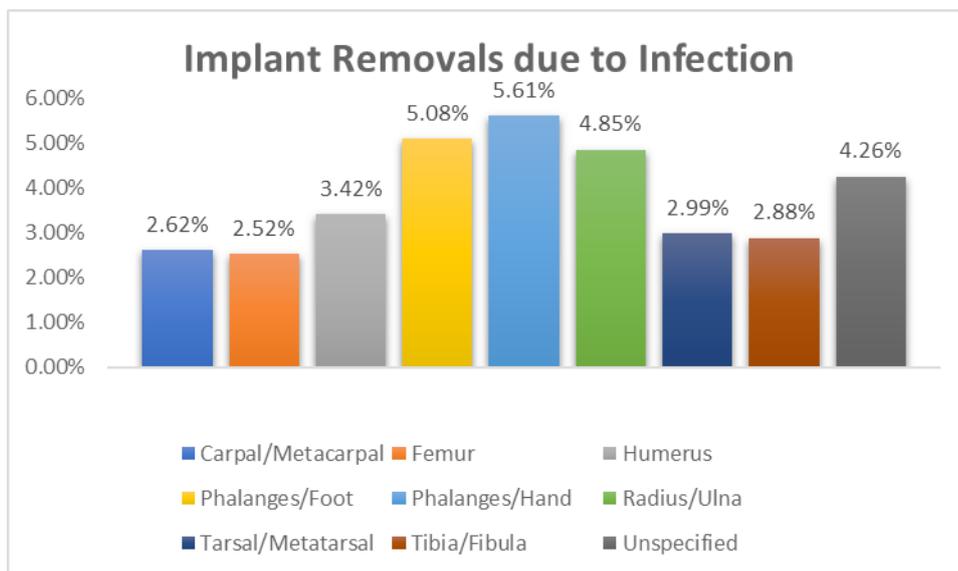


Figure 4. Implant Removals due to Infection.

Patient-Related, Hospital-Related, and Injury-Related Factors Impacting Infection-Related Hardware Removal

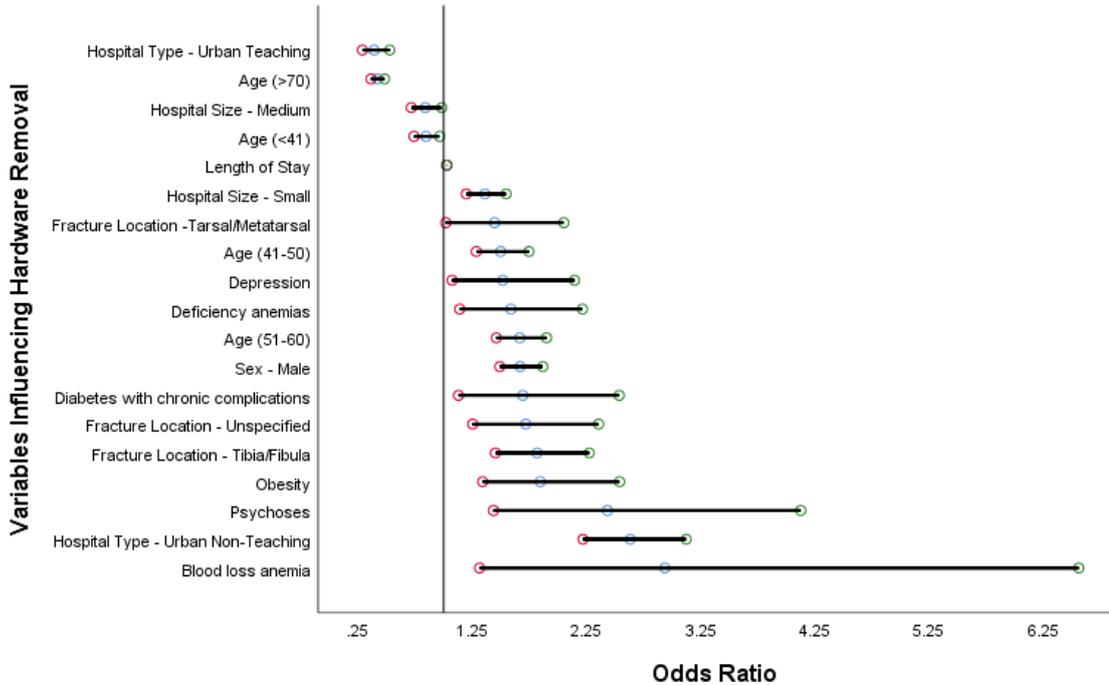


Figure 5. Predictors of infection related implant removal.

deficiency anemia (OR=1.59, 95% CI: 1.14-2.22, $P<0.01$), psychosis (OR=2.43, 95% CI: 1.44-4.13, $P<0.001$), and depression (OR=1.52, 95% CI: 1.07-2.15, $P<0.05$). Patients who were male were noted to be approximately 67% more likely to undergo removal due to infection (OR= 1.67, 95% CI: 1.49-1.87 $P<0.001$).

Length of Stay Hospital Charges

Patients undergoing removal of implant due to infection had a significantly longer length of stay (mean: 17.2) than non-infection related implant removal (mean: 9.5 days) [Figure 6]. The longest mean length of stay for infection-related implant removal was seen with carpal/

Average Length of Stay For Septic and Aseptic Implant Removal

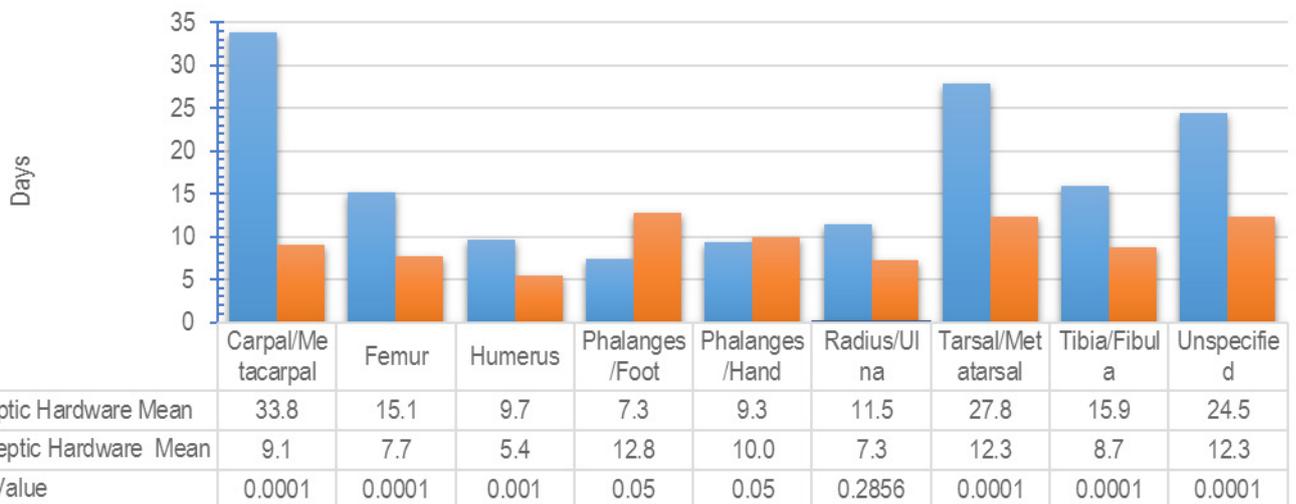


Figure 6. Average Length of Stay following Aseptic versus Septic Implant Removal.

Average Hospital Charge For Septic and Aseptic Implant Removal

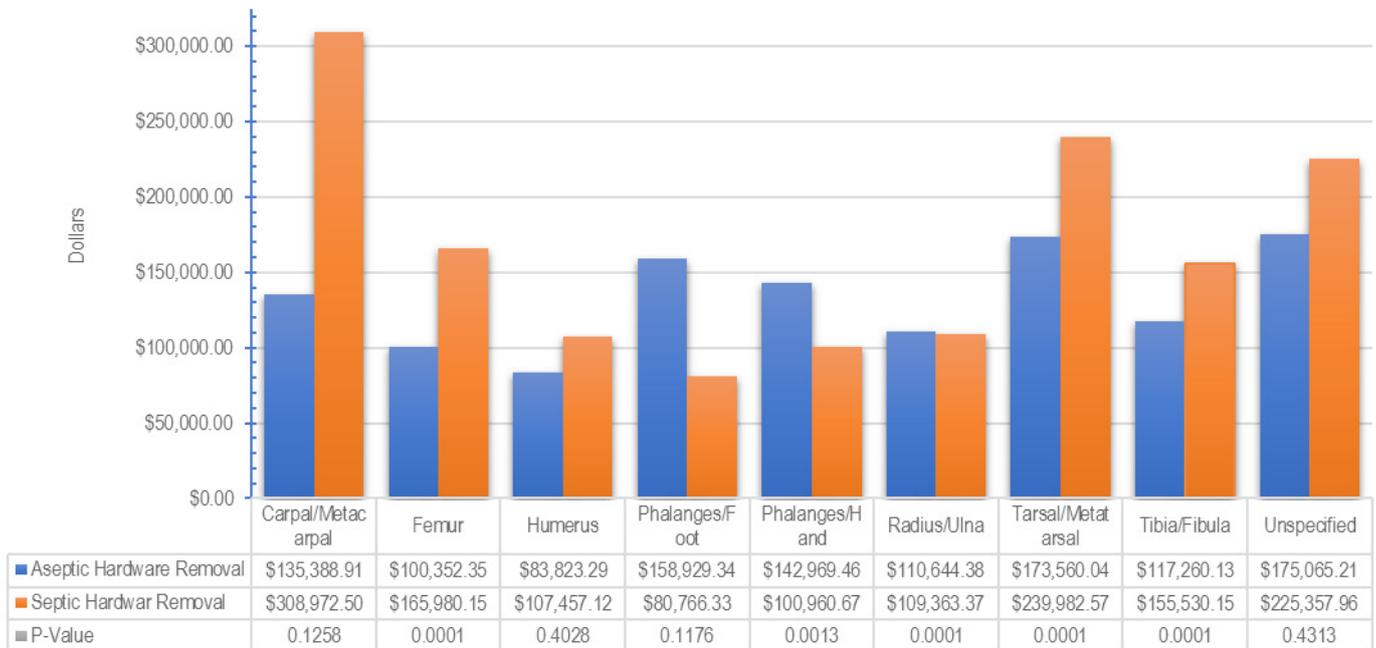


Figure 7. Hospital Charges following Aseptic versus Septic Implant Removal.

metacarpal (33.8 days), and for non-infectious implant removal was seen with phalanges/foot (12.8 days). The greatest difference in mean days for length of stay for infection-related versus non-infection related implant removal was seen between tarsal/metatarsal removals (15.5 days, 27.8 days vs. 12.3 days).

Hospital Charges

Patients undergoing removal of implant due to infection had a higher total charge associated with their episode of care (mean: \$166,041) than non-infection related implant removal (mean: \$133,110) [Figure 7]. The greatest average of total charges for infection-related implant removal was seen with carpal/metacarpal (\$308,973), and for non-infectious implant removal was seen with tarsal metatarsal (\$173,560). The greatest difference in mean total charges for infection-related versus non-infection related implant removal was seen between carpal/metacarpal removals (\$173,586, \$308,973 vs. \$135,389).

Discussion

Postoperative infection is a significant source of morbidity and mortality leading to poor functional outcomes, and places significant strain on the global healthcare system resources (24,25). Implant infections are a common complication after ORIF, but few studies have examined the trends and predictors of implant infection in these patients, with the available studies suggesting ORIF implant infection rates exceeding periprosthetic joint infection rates in arthroplasty patients(26–31). Our study investigated the patients undergoing ORIF, and the impact of infection on the need

for implant removal with the goal of determining the incidence, trends, economic burden, and predictors of implant infection following ORIF.

Complications after open reduction and internal fixation are an incredibly common postoperative problem orthopaedic surgeons contend with daily (2,28,29,32–36). While some of these complications can be managed conservatively, certain complications, such as infection or implant irritation, benefit from removal of the implant. The overall rate of implant removal is high, 13-27%, with removal of implant accounting for nearly 6% of orthopaedic procedures (37–40). One such reason for removal of implant, especially in the hands (carpal, metacarpals, and phalanges) is due to patient's feeling stiffness in the area near the implant, tendon disruption, poor healing, and infection (41). While infection can occur with any implantable device, infection of implant following ORIF is particularly devastating and can lead to significant morbidity, including amputation or permanent disability (6,7,10,42). Multiple factors contribute to a patient's risk of implant infection following ORIF, including the location of the fractures, medical comorbidities like lupus and rheumatic disease, and if the fracture was open or closed (13,29,43–45). Furthermore, comorbidities or medications that impair wound healing can further slow healing already impaired by the fracture, increasing the risk of developing a surgical site infection, implant infection, or pin site infection(33). While antibiotic therapy can treat minor infections, definitive treatment in most patients requires removal of the implant(25). Fracture location is an important variable contributing to implant infection. Lower extremity fractures, particularly

in the ankle and the tibial plateau, have incredibly high rates of postoperative wound complications (28,30). Fortunately, several studies have found the rate of implant removal and implant removal for infection, to be decreasing over the previous two decades(39,40). Our study results are in line with the literature, finding the rate of ORIF procedures, the rate of implant removal and infection-related implant removal to have decreased during the study period. Additionally, our study results were similar to the literature finding the highest removal rates due infection of the implant seen following carpal/metacarpal and phalanges/hand fracture ORIF.

The decrease in need for removal of implant, and the reduction in rate of infection-related implant is most likely due to advances and improvements in pre/peri/postoperative management of these patients. The results of our study also highlighted multiple predisposing factors to implant removal due to infection following ORIF. The medical comorbidities, including diabetes mellitus, liver disease, and rheumatoid arthritis, are well known risk factors for postoperative infection. Diabetes mellitus results is a well-known risk factor for complication due to immune dysfunction in the setting of hyperglycemic environments, and impaired wound healing (13,45). Liver disease is also a well-established risk factor for postoperative infections (46). Management of rheumatological conditions poses a nebulous decision for both the patient and the surgeon as not only can the rheumatological conditions themselves lead to increased risk of infection, the treatment modalities commonly used also can increase the risk of infection (43,47,48). These comorbidities make these patients less than ideal candidates for surgical repair, especially if treatment will be ORIF of the tibia or of tarsal fractures. However, the nature of these injuries often requires surgery for definitive management without long term functional decline and disability (49,50). The protective role of female gender being associated with decreased rates of implant removal due to infection remains controversial. Multiple studies have reported conflicting findings, with some showing female gender to decrease risk of infection, and others showing higher rates of infection (10,51-54). The role of gender is theorized to be in part to differences in sex hormone levels, particularly testosterone. Testosterone has been shown to have immune-modulatory and immune-suppressive effects, ultimately leading to a less robust antibody and immune response to infection in men than in females (55,56).

While we believe our study has the potential to have a positive impact with regards to infection-related implant removal, we understand it is not without limitations. The utilization of a national database provided a multi-year, incredibly comprehensive pool of data from institutions across the country. However, large databases have inherent errors within the systems that can lead to errors when analyzing the data (57). For this reason, the NIS was chosen in place of the American College of Surgeons National Surgical Quality Improvement Program and National Hospital Discharge Survey, as these databases have lower reports of in-hospital morbidity (58). Furthermore, there remains discrepancies between

different databases regarding incidence of injuries and procedures (16). Another limitation is the inability to capture the removal of implant in all patients undergoing this procedure as an outpatient. However, it is our belief that most patients undergoing implant removal, especially when due to infection of the implant, will have the procedure done as an inpatient. Lastly, the ICD-9 coding system does not differentiate the specific location of the ORIF procedure or removal of the implant, yielding only general locations.

Despite these limitations, we believe our study has several strengths. The main strength of our study is the review of more than 900,000 implants associated with multiple types of fractures. Our studies analyzed the trends of implant removal due to aseptic and septic indications in fracture in all the extremities. The additionally analysis of medical comorbidities, hospital factors, and financial data associated with each episode of care creates a comprehensive study that provides a comprehensive epidemiological analysis of implant removal following ORIF. The current study provides a multi-year analysis of a large national database assessing the trends in ORIF procedures, and aseptic and septic removal of implant following ORIF for eight fracture locations. The results indicate the highest rate of infection-related removal of implant is seen following ORIF of tarsal and tibial fractures. Lastly, the study reinforced the current literature indicating the increased risk of infection associated with diabetes mellitus, liver disease, and rheumatological conditions.

Implant removal rates due to infection decreased in all fractures except radial/ulnar fractures. Diabetes, liver disease, obesity, anemia, depression, and rheumatoid arthritis were significant predictors of infection-related implant removal. Identification of the trends and predictors of implant-related infection is only a first step. These medical conditions must be appropriately managed medically, and further studies investigating possible "best practice" guidelines for medical co-management and optimization of these patients are necessary in order to decrease their risk for implant-related infection.

Funding: No funding was received for this research study. We have no conflicts of interest to disclose.

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