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Original article

FREQUENCY OF SURGICAL SITE INFECTIONS FOLLOWING SURGICAL TREATMENT OF ISOLATED FRACTURES: A RETROSPECTIVE STUDY

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Abstract

Surgical site infections (SSIs) are a frequent and serious complication that occur after surgical treatment of isolated fractures, leading to increased morbidity, mortality, prolonged hospital stays, and higher healthcare costs. This study aimed to identify the frequency and risk factors associated with SSIs. Methods: This retrospective observational study included 51 patients who underwent open reduction and internal fixation (ORIF) surgery for isolated fractures and later developed bacterial infections. We analyzed factors such as the presence of comorbidity, patient age, gender, body region affected, and duration of the operation. We used multinomial logistic regression and chi-square tests as statistical analyses to examine the relationships between these factors and the types of pathogens as a cause of bacterial infection, classified as Gram-positive bacteria only, Gram-negative bacteria only, or both. Results: Our study found that in 18%, 56% and 26% of patients the cause of infection was Gram-positive, Gram-negative and both groups of bacteria, respectively. The factors that did not significantly predict the type of bacterial infection were: comorbidity presence, although the observed trends suggested further investigation was needed; duration of operation; and patient age. Gender analysis concluded a marginally significant association, with males less likely to have infections caused by Gram-positive bacteria. Additionally, the body region affected showed a marginally significant correlation with infection type, with the thigh region being more sensitive to infections caused by Gram-negatives.

Our study highlights trends and marginal associations in SSIs post-ORIF surgery, suggesting the need of personalized infection control strategies.

Keywords: surgical site infections, orthopedic surgery, isolated fractures, infection risk factors, patient outcomes

Introduction

Surgical site infections (SSIs) usually occur within 30 days after a surgical procedure, or within one year if an implant is involved, and affect the incision of the surgical site or the deep tissues[1]. These kinds of infections are linked with increased morbidity and mortality, as well as a major economic impact because of the prolonged hospital stays and higher costs of treatment[2,3]. SSIs are present in a variety of orthopedic surgeries, with studies reporting that they develop in 2–14.2% of patients after undergoing open reduction and internal fixation (ORIF), with almost half of these infections being deep infections. The variation in SSI rates depends on factors such as the type and complexity of the surgery, patient demographics, and perioperative conditions[4-7].

Various factors contribute to the risk of developing SSIs after fracture surgery, as highlighted in the studies of Li *et al*., which include patient's age, the presence of comorbidities, older age, duration of the operation, and type of the fracture treated[4,8]. Studies by Mangram *et al.* and Berrios *et al.* have shown that the prolonged duration of the surgery increases the risk of wound exposure to potential bacteria, while massive blood loss can lower immune function and wound healing, thereby showing the need of efficient surgical operations and effective blood management strategies to reduce the risk of SSIs[1,9]. Additionally, the study by Korol *et al.* revealed that the type of fracture and the presence of implants can influence the risk, with open fractures and extensive internal fixation showing higher infection rates due to the increased complexity of the procedure and longer operating times, which further worsen the risk of infection[8].

Preventive measures are crucial in minimizing the risk of SSIs, as shown in studies by Korol *et al.* and Klevens *et al.* where administering prophylactic antibiotics within one hour before surgery significantly lowered the likelihood of SSIs, optimized their effectiveness and enhanced overall surgical outcomes[8,10]. Furthermore, proper surgical techniques are critical for minimizing the risk of SSIs. This includes accurate debridement to remove devitalized tissue and thorough irrigation of wounds to reduce bacterial load, both of which are critical in preventing infection[9,11].

The microbiological profile of SSIs in orthopedic surgery is also important. The literature shows that the most common pathogen isolated from these infections is *Staphylococcus aureus,* including methicillin-resistant strains (MRSA), as it was elaborated in the study by Lentino *et al.* to be primarily cause of prosthetic joint infections, highlighting the significant challenge these resistant strains pose to effective treatment[12]. Similarly, the prospective study by Zhang *et al*. on plateau tibial fractures treated with open reduction and internal fixation found that *Staphylococcus aureus,* including MRSA, was the most frequent pathogen, but also with significant involvement of Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* in these infections[4]. The understanding of the microbial profile is essential for selecting appropriate antibiotic prophylaxis and treatment strategies, as it has been described in the study by Phillips *et al.* that accurate identification of specific microorganisms is crucial for choosing the best empiric antibiotic therapies and improving patient result[13]. Furthermore, the systematic review by Korol *et al.* showed that adjusting antibiotic prophylaxis to the local microbial and resistance patterns significantly enhanced the effectiveness of infection control measures, thereby optimizing SSI prevention and management[8]. This approach not only targets the specific bacteria but also helps with antibiotic resistance by ensuring targeted and effective treatment strategies.

The culture-free methods, such as immunoassays and nucleic acid amplification tests, are very important in accurately identifying the microbial burden in wounds. According to the World Health Organization (WHO) these methods offer a more comprehensive understanding of the infection compared to traditional culture techniques on preoperative measures for SSI prevention, which improve detection accuracy, enabling targeted antibiotic therapy and better infection control[11,14].

Overall, the prevention and management of SSIs following surgical treatment of isolated fractures remains an important challenge that requires future research to focus on identifying and lowering risk factors for SSIs to further improve surgical outcomes in patients with fractures. Given the variability in SSI rates and contributing factors, a tailored approach to infection control and prevention is essential in orthopedic practice[10,15].

Methods

Study design

This retrospective observational study analyzed the impact of different factors on the type of bacterial infections that were detected in surgical patients hospitalized at the University Clinical Center for Traumatology, Orthopedics, Anesthesia, Reanimation, and Intensive Care and Emergency Medicine (TOARILUC) in Skopje from September 2021 to March 2023. The study included patients with isolated fractures who presented with signs of infection. Patients included in the study were aged 18-75 years, had closed fractures, underwent orthopedic-traumatological surgeries with implant placement, and exhibited clinical signs of infection, while those excluded were patients with open fractures, new trauma at the surgical site and those on immunosuppressive therapy. Patients were informed about the objectives of the study and they provided written consent for participation. The factors included were comorbidity presence, patient age, gender, body region affected by the surgical procedure, and duration of the operation. This study aimed to identify major cause of postoperative SSIs classified into three groups: Gram-positive bacteria, Gram-negative bacteria and both.

Participants

Over a period of 18 months, a total of 2800 patients were analyzed. The study included patients who underwent ORIF surgery for isolated fractures and postoperatively developed wound infections. Wound infections were detected in 51(1.82%) of these patients, most commonly affecting the skin and subcutaneous tissue. Data were collected from this cohort of 51 surgical patients focusing on those who developed bacterial infections post-operation. There were no missing cases in the data.

Data Collection

The dependent variable, type of bacterial infection, was categorized into three groups for analysis, coded as 0 for Gram-positive bacteria, 1 for Gram-negative bacteria and 3 for both. The independent variables included:

Comorbidity Presence: Coded as 0 for no and 1 for yes.

Patient Age: Continuous variable defining the age of the patient.

Gender: Coded as 0 for female and 1 for male.

Body Region Affected: Classified as 1=Upper Arm/Hand, 2=Forearm, 3=Spine, 4=Thigh, 5= Lower Leg, 6=Foot, and 7=Pelvis.

Duration of Operation: Continuous variable defining the time in minutes.

Microbiological analysis

For patients with signs of surgical site infection, swab samples were taken from the wound for microbiological testing and sent for analysis to the Institute of Microbiology and Parasitology, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje. On receipt by the laboratory, all specimens were inoculated onto standard agar media (Columbia agar with 5% sheep blood for the isolation of aerobes, Schaedler agar for the isolation of anaerobes and glycose broth). The aerobic plates were read within 24–48 hours and the anaerobic plates at 48 and 72 hours. Any growth was subsequently identified by standard microbiological methods, i.e., the appearance of the colonies, biochemical identification and automated Vitek 2 system. Automatized Vitek system (bioMerieux, Marcy l'Etoile, France) was used for confirmation of isolated bacteria, using VITEK ID cards. The VITEK 2 system reported the results automatically with software release 2.01 according to manufacturer's recommendations. Quantitative bacteriology was not performed. Gram-stained smears from wound specimens were also performed at the time of culturing, in which the presence of bacteria and/or leukocytes (Le) was detected. Determination of the susceptibility of isolated bacteria was done using standard disk diffusion method and for the interpretation of the results, EUCAST criteria were used. For all strains which were resistant to antimicrobial agents by disk diffusion method, Vitek system was used for the confirmation of the resistance, using VITEK AB cards. Results were reported as S (susceptible), I (intermediate susceptible) and R (resistant) according to standard disk diffusion method and as MIC values according to VITEK System for susceptibility testing.

Statistical Analysis

A multinomial logistic regression was used to determine the relationships between the independent variables and the type of bacterial infection, with Gram-negative only serving as the reference category. The model's fit and the significance of predictors were evaluated using Chi-Square tests and Likelihood Ratio tests. Additionally, the Chi-Square test of independence was used to assess the association between categorical variables such as body region and infection type, and comorbidity presence and infection type.

Results

Participant characteristics

Of all the analyzed patients, 9(18.0%) had infection caused by Gram-positive bacteria, 28 (56.0%) had infection caused by Gram-negatives, and 13(26.0%) had infection caused by both groups of bacteria.

Acinetobacter spp. (whether in combination or alone) was the most frequently isolated bacteria, appearing in 18 samples, accounting for 35.3% of the total isolates. However, *Pseudomonas spp.* (whether in combination or as a single isolate) was the second most frequently isolated bacteria, found in 14 samples, representing 27.5% of the total isolates. One sample contained *Fusarium*, a fungal isolate, which was excluded from the bacterial analysis.

Gram-negative bacteria included *Acinetobacter spp., Pseudomonas spp., Enterobacter spp., Klebsiella pneumoniae, Escherichia coli, Providencia stuartii, Stenotrophomonas maltophilia,* and *Proteus mirabilis*. These constituted the majority of isolates. Gram-positive bacteria included *Staphylococcus aureus* (including MRSA), *Staphylococcus* coagulase-negative, *Corynebacterium* group JK, *Streptococcus pyogenes* group A, and *Enterococcus spp*.

The median frequency of bacterial isolates was 2, indicating that half of the bacterial isolates occurred in combination with another bacteria. The mode for bacterial frequency was 1, showing that most bacteria were found as a single isolate or in combination with other bacteria.

Comorbidity presence

The multinomial logistic regression analysis for comorbidity presence indicated that this variable did not significantly explain the variability in the cause of bacterial infection. The final model showed a -2 Log Likelihood of 12.692 with a Chi-Square of 3.561 (df=2, p=.169), indicating no statistically significant improvement in fit over the intercept-only model. Pseudo R-square values were low (Cox and Snell: 0.069; Nagelkerke: 0.080; McFadden: 0.036), demonstrating a minimal explanatory power. The likelihood ratio tests indicated that comorbidity presence was not a statistically significant predictor (Chi-Square=3.561, df=2, p=0.169). Comorbidity presence had a marginally significant association with the likelihood of having both Gram-negative and Gram-positive bacterial infection (B=0.470, p=.492), although this was not statistically significant. However, the results suggested a trend worth further investigation, particularly the marginally significant association with the likelihood of having both Gram-negative and Gram-positive bacterial infection (B=0.470, p=.492).

Table 1. Detailed Multinomial Logistic Regression Analysis by Comorbidities

Predictor	Infection Type Comparison	Coefficient (B)	Std. Error	Wald Chi-Square	p-Value	Exp(B) (Odds Ratio)	95% Confidence Interval
Intercept	Gram-Positives only (Reference)	-0.693	0.463	2.242	0.134	None	None
Comorbidity Presence	Gram-positives only *vs.* Gram-negatives only	-1.253	0.886	1.997	0.158	0.286	(0.050, 1.642)
Intercept	Both Gram-negatives and Gram-positives	-1.030	0.521	3.906	0.048	None	None
Comorbidity Presence	Both *vs.* Gram-negatives only	0.470	0.684	0.472	0.492	1.600	(0.419, 6.115)

Duration of operation

Similarly, the duration of operation did not significantly predict the cause of bacterial infection. The final model showed a -2 Log Likelihood of 37.705 with a Chi-Square of 0.633 (df =2, p=0.729), indicating no statistically significant improvement over the intercept-only model. Goodness-of-fit measures indicated the model did not fit the data well (Pearson Chi-Square:

Table 2. Multinomial Logistic Regression Analysis of Factors Influencing on Type of Bacterial Infections by Operation Duration

Predictor	Infection Type Comparison	Coefficient (B)	Std. Error	Wald Chi-Square	p-Value	Exp(B) (Odds Ratio)	95% Confidence Interval
Intercept	Gram-Positive Only (Reference)	-1.183	0.581	4.145	0.042	None	None
Duration of Operation	Gram-Positive Only vs. Gram-Negative Only	0.000	0.004	0.012	1.000	1.000	(0.992, 1.008)
Intercept	Both Gram-Negative and Gram-Positive	-0.441	0.573	0.593	0.441	None	None
Duration of Operation	Both vs. Gram-Negative Only	-0.004	0.005	0.447	0.447	0.996	(0.986, 1.007)

16.260, df=18, p=0.574; Deviance: 19.308, df=18, p=0.373). Pseudo R-square values were low (Cox and Snell: 0.013; Nagelkerke: 0.015; McFadden: 0.006), indicating a minimal explanatory power. The likelihood ratio tests indicated that the duration of operation was not a statistically significant predictor (Chi-Square=0.633, df=2, p=0.729).

Patient age

The analysis of patient age revealed that it did not significantly predict the cause of bacterial infection. The final model showed a -2 Log Likelihood of 84.622 with a Chi-Square of 0.215 (df=2, p=0.898), indicating no statistically significant improvement in fit over the intercept-only model. The pseudo-R-square values were very low (Cox and Snell: 0.004; Nagelkerke: 0.005; McFadden: 0.002), demonstrating a minimal explanatory power. The likelihood ratio tests indicated that patient age was not a statistically significant predictor (Chi-Square=0.215, df=2, p =0.898).

Table 3. Multinomial Logistic Regression Analysis of Factors Influencing on Type of Bacterial Infections by Age

Predictor	Infection Type Comparison	Coefficient (B)	Std. Error	Wald Chi-Square	p-Value	Exp(B) (Odds Ratio)	95% Confidence Interval
Intercept	Gram-Positive Only (Reference)	-0.679	1.091	0.387	0.534	None	None
Age of the Patient	Gram-Positive Only vs. Gram-Negative Only	-0.009	0.020	0.193	0.860	0.991	(0.953, 1.031)
Intercept	Both Gram-Negative and Gram-Positive	-0.525	0.978	0.288	0.591	None	None
Age of the Patient	Both vs. Gram-Negative Only	-0.005	0.018	0.069	0.793	0.995	(0.962, 1.030)

Gender

The analysis of gender revealed a marginally significant association between gender and the cause of bacterial infection. The final model had a -2 Log Likelihood of 12.744 with a Chi-Square of 5.514 (df=2, p=.063), indicating a trend that males are less likely to have Gram-positive bacterial infection compared to females (B=-1.792, p=.031). This finding highlights the

Table 4. Multinomial Logistic Regression Analysis of Factors Influencing on Type of Bacterial Infections by Gender

Predictor	Infection Type Comparison	Coefficient (B)	Std. Error	Wald Chi-Square	p-Value	Exp(B) (Odds Ratio)	95% Confidence Interval
Intercept	Gram-Positive Only (Reference)	-0.154	0.556	0.077	0.782	None	None
Gender (Male=1)	Gram-Positive Only vs. Gram-Negative Only	-1.792	0.831	4.650	0.031	0.167	(0.033, 0.859)
Intercept	Both Gram-Negative and Gram-Positive	-0.154	0.556	0.077	0.782	None	None
Gender (Male=1)	Both vs. Gram-Negative Only	-0.944	0.707	1.784	0.182	0.389	(0.097, 1.558)

importance of considering gender as a factor in post-operative infection management.

Body region affected

The Chi-Square tests for the body region affected indicated a marginally significant association between the body region and the cause of bacterial infection. The Pearson Chi-Square value was 19.651 (df=12, p=.076), suggesting that certain body regions, such as thigh and spine, had higher occurrences of specific types of bacterial infection. This result underscores the need for tailored infection control strategies based on the surgical site.

Table 5. Distribution of Bacterial Infections Across Body Regions

Body Region	Gram-Positive Only	Gram-Negative Only	Both
Upper Arm/Hand	0	2	0
Forearm	1	0	1
Spine	0	3	3
Thigh	4	1	12
Lower Leg	4	6	8
Foot	0	0	2
Pelvis	1	0	2

Table 6. Chi-Square Test Results for Body Region

Test	χ^2	df	p-Value
Pearson Chi-Square	19.651	12	0.076
Likelihood Ratio	19.569	12	0.074
Linear-by-Linear Association	2.376	1	0.123

Cross-tabulation and Chi-Square Analysis

The cross-tabulation analysis provided detailed insights into the distribution of bacterial infection types across different categories of the independent variables. For instance, patients with comorbidities had a slightly higher occurrence of Gram-negative bacterial infection. Similarly, the distribution of infection across different body regions showed significant variation, with the thigh region being particularly prone to bacterial infection caused by Gram-negatives.

Table 7. Cross-tabulation of bacterial infections by comorbidity presence

Comorbidity Presence	Gram-Positive Only	Gram-Negative Only	Both	Total
No	7	14	5	26
Yes	2	14	8	24
Total	9	28	13	50

Table 8. Chi-square test results for comorbidity presence

Test	χ^2	df	p-Value
Pearson Chi-Square	3.396	2	0.183
Likelihood Ratio	3.661	2	0.169
Linear-by-Linear Association	3.015	1	0.083

Directional measures

Directional measures such as Lambda and Goodman and Kruskal tau indicated weak but notable associations between the independent variables and bacterial infection types. For example, Lambda (Symmetric) for comorbidity presence was .065 (Asymptotic Standard Error: .075), and Goodman and Kruskal tau (Symmetric) was .068 (Asymptotic Standard Error: .066). These measures suggest that while the associations are not strong, they are still worth considering in the broader context of infection control and prevention.

Table 9. Directional measures for comorbidity presence

Measure	Value	Asymptotic Standard Error	p-Value
Lambda (Symmetric)	0.065	0.075	0.075
Lambda (Comorbidity Dependent)	0.125	0.141	0.141
Lambda (Bacteria Dependent)	0.000	0.000	0.000
Goodman and Kruskal tau (Symmetric)	0.068	0.066	0.065
Goodman and Kruskal tau (Comorbidity Dependent)	0.024	0.024	0.024
Goodman and Kruskal tau (Bacteria Dependent)	0.000	0.000	0.000
Uncertainty Coefficient (Symmetric)	0.042	0.043	0.043
Uncertainty Coefficient (Comorbidity Dependent)	0.051	0.052	0.052
Uncertainty Coefficient (Bacteria Dependent)	0.036	0.036	0.036

Discussion

The findings obtained in our study provide important insights into the factors influencing the frequency and the cause of SSIs following ORIF surgery for isolated fractures. The analysis highlights the multifactorial nature of SSIs and aligns with existing literature on the subject.

The presence of comorbidities is known to play a significant role on the incidence of SSIs. Our study found that while comorbidities were not statistically significant predictors of the type of bacterial infection (p=0.169), the trends observed suggest a potential role in influencing infection risk. Patients with comorbidities had a slightly higher occurrence of Gram-negative bacteria as a cause of infection. Comorbidities such as diabetes, obesity, and immunosuppressive conditions significantly impair immune response and wound healing, thereby increasing susceptibility to infections as described in the study by Weigelt *et al.,* which demonstrated that diabetes and obesity were critical risk factors for SSIs due to their negative role on wound healing [16]. Similarly, the study by Berbari *et al.* found that patients with rheumatoid arthritis and those undergoing immunosuppressive therapy were at a higher risk of SSIs because their compromised immune systems were less effective in combating infections[17].

Our analyses showed no significant correlation between patient age and type of bacterial infection (p = 0.898). This finding aligns with existing literature, where the association between age and SSIs is inconsistent. The study by Geubbels *et al.* reported that older patients might be at a higher risk due to lower immune response and compromised skin integrity, which can impair wound healing and increase risk of infections[18]. However, the study by Anthony *et al*. found that age was not a significant independent predictor of SSIs when controlling for other variables, suggesting that the risk of SSIs was multifactorial and not solely dependent on age[19]. Improving risk-adjusted measures of SSIs is crucial, as age alone may not be a strong predictor without considering other variables; this is supported by findings indicating that while age could be associated with increased SSI risk in some procedures, the effect is often mediated by factors such as comorbidities and the nature of the surgical intervention, and that SSI rates vary significantly by wound class, surgical procedure, and patient risk index, underscoring the need to consider age alongside other risk factors for a comprehensive assessment[20-22].

The analysis concluded a marginally significant correlation between gender and type of bacterial infection, with males showing a lower likelihood of Gram-positive bacterial infection compared to females (p=0.063). This is consistent with the study by Darouiche *et al*., who reported gender differences in SSI rates, potentially due to variations in skin flora and hormonal influences[23]. Moreover, a study by Aghdassi *et al*. analyzed data from the German national hospital-acquired infection surveillance system and found that male patients undergoing orthopedic and abdominal surgery were more likely to develop SSIs compared to female patients, while females had higher rates of SSIs following heart and vascular surgeries[24]. This underscores the complexity of gender-related risk factors in SSIs and the necessity for tailored preventive strategies.

The Chi-Square tests indicated a marginally significant association between the body region affected and type of bacterial infection (p=0.076). Specifically, the thigh region showed a higher occurrence of Gram-negative bacteria as a cause of infection. This observation aligns with findings that certain body regions are more susceptible to specific bacteria due to differences in vascularity and tissue type. Studies have shown that areas with higher blood flow and dense tissue structures provide an optimal environment for the proliferation of Gram-negative bacteria[25]. SSIs are most frequently observed in regions like the abdominal cavity, where procedures often involve exposure to the gastrointestinal tract, leading to a higher likelihood of contamination by Gram-negative bacteria[1]. Additionally, infections in the lower extremities, especially in cases involving orthopedic implants, are predominantly associated with Gram-positive bacteria due to the presence of skin flora[2].

Prolonged surgical duration is a known risk factor for SSIs. Longer surgeries increase the risk of SSIs as it was found in a study by Cheng *et al.* showing that each additional hour of surgery increased the risk of SSIs by approximately 30% (26). Extended operative times can also impair the patient's immune response due to factors like prolonged anesthesia and intraoperative hypothermia, which are associated with increased postoperative complications, including infections[3]. Additionally, complex surgeries, which typically last longer, are associated with a higher incidence of SSIs, as demonstrated by Procter *et al.*[27]. Our study, however, did not find a statistically significant relationship between the duration of operation and type of bacterial infection (Chi-Square=0.633, df=2, p=.729), suggesting that other factors may play a more critical role.

Our study has several limitations. The most significant limitation is the small sample size, which may limit the generalizability of our findings. Additionally, the single-center design and retrospective nature restrict control over confounding variables, and long-term follow-up data were not included. These limitations highlight the need for larger, multi-center, prospective studies to validate and expand upon these findings.

Conclusion

This study highlights the potential for personalized infection control strategies in orthopedic surgeries to significantly reduce the incidence of SSIs by considering factors such as comorbidities, duration of operation, gender, age, and body region. Despite some variables not independently predicting the type of bacterial infection, the observed trends and marginally significant associations point to promising areas for further research and the development of tailored preventive measures, such as including one-hour preoperative antibiotic prophylaxis, which is essential to improve patient outcomes and reduce infection rates.

Conflict of interest statement. The authors declare no conflict of interest.

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