Microbiology and Risk Factors of Surgical Site Infection in Limb Fractures

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Abstract

Background: Limb fractures are becoming more common, and implant implants increase the risk of surgical site infection. The purpose of this study was to identify risk factors and microbiological characteristics for surgical site infection of limb fractures.

Methods: We reviewed the data of 4,478 patients with limb fractures treated at Zhejiang Provincial People's Hospital from January 2010 to January 2020, including demographic, fracture, and microbiological characteristics. Chi-square tests and multivariate logistic regression were used to identify risk factors.

Results: *Staphylococcus aureus* is a major threat to surgical site infection of limb fractures (26.46%). Open fractures are a risk factor for gram-negative infections. The following factors are considered as risk factors for surgical site infection: lower limb fractures, diabetes mellitus (OR 2.911 ; 95% CI 1.767-4.793), hypoproteinemia (OR 5.153 ; 95% CI 2.478-10.714), vascular injury (OR 8.531 ; 95% CI 4.028-18.070), nerve injury (OR 1.966 ; 95% CI 1.132-3.414) and open fractures (OR 9.561 ; 95% CI 6.565-13.925).

Conclusions: Patients with these factors are at risk of surgical site infection after open reduction and internal fixation, and orthopedic surgeons should pay attention to these patients.

Introduction

Limb bones are more vulnerable to the violence that causes fractures than axial and skull bones. In recent years, the treatment of limb fractures has been improving, for example, by designing longer steel plates and intramedullary nails, and improving the coating of internal plant surfaces to reduce complications such as osteoporosis, nonunion, and posttraumatic bone defects.[1] However, post-implantation infection is still an important problem for orthopedic surgeons.

Deep surgical site infection (SSI) is defined as an infection that occurs in the fascia, muscle layer, or any part of the body that is opened during surgery. On average, SSI extended hospital stays by 9.7 days and increased the cost of each hospitalization by \$20,000. [2] Orthopaedic surgery poses a greater risk of infection than other procedures without implant implants. Microorganisms commonly associated with orthopedic SSI, such as *Staphylococcus aureus* (*S. aureus*) and *Staphylococcus epidermis* (*S. epidermis*), can adhere to the surface of internal plants and form biofilms to resist the infiltration of antibiotics. [3] At the same time, the presence of implant tends to make the infection more chronic, stimulating the formation of granulation tissue and the formation of fibrous encapsulation. [4]

Identified the microbiological characteristics of different limb fractures and risk factors for SSI is important to infection prevention. Continuous infection surveillance has been used worldwide for infection prevention. [5] In this study, we evaluate the microbiological characteristics and incidence of SSI for limb fractures and to identify risk factors.

Methods

We reviewed the data of patients with limb fractures who underwent surgery at Zhejiang Provincial People's Hospital from January 1, 2010 to January 1, 2020. This 1800-bed university affiliated hospital, with a 219-bed Orthopedic Service, served a total population of about 1000,000 people.

We accessed the database of hospital and screened out 4478 patients meeting the inclusion. Next, four physicians recorded data of each patients, including gender, age, hypertension, diabetes, hypoproteinemia, nerve injury at the fracture site, vascular injury at the fracture site, skin injury, wound type, infections, infecting microorganisms and drug sensitivity test results.

SSI was defined according to a standard 2008 Centers for Disease Control and Prevention (CDC) definition.[6] The infection occurring within 1 year after implantation was defined as SSI. All SSIs detected during hospitalisation, readmission and post-discharge outpatient visit were included.

Potential risk factors associated with SSI were analyzed using a univariate and multivariate models. Rate and categorical variables were compared by chi-square test with values of $P < 0.2$ considered to be potential independent variables, and entered into the logistic regression model. The variables of two-tailed $P < 0.05$ were included in final model. Statistical analysis was conducted with the SPSS program version 23.0 (IBM Corp., Armonk, NY).

Results

The characteristics of the patients were shown in Table 1. A total of 187 patients with limb fractures treated with internal fixation had surgical site infection.

Table 1
Baseline characteristics of study patients

Characteristic	SSI (n = 187,4.2%)	No SSI (n = 4291,95.8%)
Age, year, mean $\pm$ SD	51.01, 18.22	51.27, 18.65
Male, n(%)	128 (68.4)	2464 (57.4)
Hypertension, n(%)	29 (15.5)	665 (15.4)
Diabetes mellitus, n(%)	23 (12.8)	274 (6.3)
Hypoproteinemia, n(%)	13 (6.9)	57 (1.3)
Fracture site, n(%)		
Humerus	10 (5.3)	544 (12.6)
Ulna and Radius	9 (4.8)	1030 (23.0)
Femoral	43 (22.9)	865 (20.1)
Patella	14 (7.4)	384 (8.9)
Tibia and Fibula	94 (50.2)	1062 (24.7)
Foot	17 (9.0)	406 (9.4)

Microbiology:

The microorganism most frequently isolated from infected surgical wounds is *S. aureus* (26.46%), followed by *Acinetobacter baumannii* (AB) (12.23%) and *Pseudomonas aeruginosa* (PA) (10.05%). In our study, the infection rate for lower limb fractures is significantly higher than that for upper limb fractures (3.75% vs. 0.42%), so we compare surgical site infections of the humerus, radius, and ulna under one category. After adjusting for age, sex and other confounders, the distribution of gram-negative and gram-positive bacteria in different limb fractures is similars ($P > 0.2$). [Figure 1]

Figure 1: The distribution of microorganisms in limb fractures. We defined microorganism with frequencies less than 6 times as rare microorganisms.

In orthopaedic common antibiotics, *S. aureus* is sensitive to Levofloxacin and Moxifloxacin. Moxifloxacin has a good effect on *S. epidermis* and *Streptococcus hemolyticus* (*S. hemolyticus*). AB has poor sensitivity to most antibiotics and Cefoperazone / Sulbactam is the most effective antibiotic. Most antibiotics are effective against *Pseudomonas aeruginosa*. *Klebsiella pneumoniae* (KP) is the most sensitive to Cefotaxime. In addition to Ceftriaxone, other antibiotics have a good effect on *Escherichia coli* (*E. coli*). [Table 2]

Table 2
Sensitivity of common antibiotic

Microorganism	Cases (%)	Sensitive rate (%)						
		Vancomycin	Tigecycline	Linezolid	Levofloxacin	Moxifloxacin	Clindamycin	Oxacillin
S. aureus	26.7	100	100	97.96	61.12	60.42	46.94	38.78
S. epidermidis	8.6	100	100	100	50	78.57	42.86	7.14
S. hemolyticus	7.0	100	100	100	27.27	58.33	27.27	0
		Piperacillin / tazobactam	Cefoperazone/sulbactam	Amikacin	levofloxacin	Cefotaxime	Ceftazidime	Ceftriaxone
AB	13.7		39.13	34.62	12.50		16.67	
PA	10.2	100	84.62	94.74	94.74		88.24	
KP	4.8	44.44	50	66.67	50	87.50	42.86	25
E.coil	5.3	100	100	88.89	50		71.43	11.11

Risk factors:

In order to determine limb fracture infection and risk factors affecting the distribution of gram-negative and gram-positive bacteria, we further treated multiple taxonomic variables. Since there were fewer patients with limb fractures under the age of 10 in this hospital, we divided the patients into three groups: $0 < \text{age} \leq 30$, $30 < \text{age} \leq 50$, and $50 < \text{age}$. The results showed that advanced age did not increase the risk of SSI, nor did it affect the distribution of gram-negative and gram-positive bacteria ($P > 0.05$).

Multivariate Logistic regression analysis suggests that wound type and vascular injury at the fracture site can influence the distribution of gram-negative and gram-positive bacteria. Open fractures (adjusted OR = 2.945 ; 95% CI 1.529–5.674) and vascular injury at the fracture site (adjusted OR = 2.624 ; 95% CI 1.058–6.505) are risk factors for gram-negative bacteria infection. In this study, we also analyze the effect of soft tissue injury on the distribution of gram-negative and gram-positive bacteria in closed fractures and found that soft tissue injury alone do not increase the risk of gram-negative bacteria infection ($P > 0.05$).

The risk factors associated with SSI by Multivariate Logistic regression analysis are shown in Table 3. Included variables included fracture site, diabetes mellitus (adjusted OR = 2.911 ; 95% CI 1.767–4.793), hypoproteinemia (adjusted OR = 5.153 ; 95% CI 2.478–10.714), vascular injury at fracture site (adjusted OR = 8.531 ; 95% CI 4.028–18.070), nerve injury at fracture site (adjusted OR = 1.966 ; 95% CI 1.132–3.414) and wound type (adjusted OR = 9.561 ; 95% CI 6.565–13.925). There is a lower risk of infection in the humerus (adjusted OR = 0.286 ; 95% CI 0.117–0.697), ulnar and radius (adjusted OR = 0.222 ; 95% CI 0.092–0.539), and an increased risk of infection in the femur (adjusted OR = 1.426 ; 95% CI 0.751–2.707), tibiofibula (adjusted OR = 2.073 ; 95% CI 1.156–3.716) and patella (adjusted OR = 1.445 ; 95% CI 0.669–3.120), compared to fractures in the foot.

Table 3
Multivariate analysis of risk factors associated with SSI

Variable	P value	Odds ration	95% CI
Fracture site			
Humerus	0.006	0.286	0.117–0.697
Ulnar and Radius	0.001	0.222	0.092–0.539
Tibia and Fibula	0.014	2.073	1.156–3.716
Diabetes mellitus	<0.001	2.911	1.767–4.793
Hypoproteinemia	<0.001	5.153	2.478–10.714
Vascular injury	<0.001	8.531	4.028–18.070
Nerve injury	0.016	1.966	1.132–3.414
Wound type	<0.001	9.561	6.565–13.925

Discussion

Consistent with previous studies, *S. aureus* is the greatest threat to orthopedic SSI. *S. aureus* is continuously colonized in the anterior nasal in about 20% of the population and intermittently colonized in up to 60%. [7, 8] Past studies have found that prophylaxis by temporarily removing *S. aureus* colonized in the anterior nasal passage before surgery or by giving antibiotics to patients screened for positive *S. aureus* colonizations can effectively reduce the risk of SSI. [9, 10] Ran Schwarzkopf and his colleagues found that *S. aureus* colonized the anterior nasal of orthopaedic surgeons at a higher rate than patients who received joint replacement and spinal surgery, revealing a potential risk factor.[11] *S. aureus* has ability to attach to implants. [12] Osteomyelitis is a serious consequence of *S. aureus* infection. The classic mechanism of *S. aureus* causing osteomyelitis includes four steps:(1)abscess formation;(2)biofilms formation;(3)invasion of the osteocyte lacuno-canalicular network (OLCN) of bone;(4) intracellular infection.[13] The formation of biofilms is an important step in staphylococcus aureus infection, which limits access of antibiotics to microorganisms. In our study, the sensitivity of *S. aureus* to methicillin is only 38.78%, far lower than the results of foreign surveys in the same period. [14, 15] The proportion of drug-resistant bacteria is on the rise worldwide, suggesting the importance of developing countries in controlling the growth of microbial resistance. In recent years, there have been improvements in measures to prevent SSI in orthopaedic, such as the use of implants with antimicrobial coatings, but this has also increased the risk of developing drug-resistant bacteria. [16]

There have been few studies on the association between AB and PA and orthopedic SSI in the past. In our study, AB and PA are significantly more distributed in open fractures than in closed fractures, suggesting an increased risk. AB is a common infection in intensive care units. As an opportunistic pathogen, AB mainly affects people with low immunity. [17] The symptoms it causes are usually milder than those of *S. aureus*. Compared with other hospitals, the proportion of critically ill patients admitted to this hospital is not significantly higher, and we suggest that limb fractures may be a potential risk factor for AB infection. Similar to *S. aureus*, PA can also form biofilms. Recently, Guoqi Wang and his collegus found that negative-pressure wound therapy can treat treat infections caused by PA. [18]

We find that the distribution of gram-negative and gram-positive bacteria is similar among different limb fractures, suggesting that we may be able to view limb fractures as a whole in terms of microbial composition. Open fractures and vascular injury at fracture site increase the risk of contamination of the wound, and thus more likely to cause infection with gram-negative bacteria.

The basic physical condition play an important role in the postoperative recovery of patients with limb fracture. Consistent with past studies, diabetes and hypoproteinemia increase the risk of infection after fracture surgery [19, 20]. High blood sugar provides a breeding ground for microbes to grow, while low protein can delay healing of surgical incisions. Albumin supplementation through diet is easier to maintain than intravenous infusion. Recent study suggests that preoperative enteral protein powder supplementation in patients with hypoproteinemia who recieve hip replacement reduces SSI rates and readmission rates [21].

The immunity and surgical wound healing ability of the elderly patients are decreased compared with the younger patients. Interestingly, in this study, we do not find that advanced age increased the risk of SSI. After reviewing the treatment measures in the hospital, we find that elderly patients tend to receive more care, such as additional use of forced-air warming system for warmth, albumin supplementation to a higher level before surgery, and more frequent dressing changes, which may have played a protective role.

Soft tissue injury, vascular injury and nerve injury at fracture sites are important problems that orthopedic surgeons pay close attention to. Our study shows that open fractures, vascular injury and nerve injury at fracture site all increase the risk of SSI. Nerve injury may make the patient insensitive to painful stimuli and reduce the protection of the surgical site. Patients with lower limb fractures have a higher risk of infection than those with upper limb fractures, which may be associated with longer bed time. Tibiofibula and patella have less soft tissue coverage, making the wound more likely to become contaminated during trauma.They are also more likely to develop skin tension after surgery.This may account for their higher risk of infection.

Although we have reviewed a long period of time, the multicentre study is still beneficial.

Conclusion

Different limb fractures may be viewed as a whole in terms of microbial composition. Open fractures increase the risk of gram-negative infections, but soft tissue damage alone does not. Diabetes and hypoproteinemia increase the risk of SSI.Vascular injury at surgical site infection, nerve injury at surgical site infection and open fractures increase the risk of SSI. Lower limb fractures are associated with a higher risk of infection than upper limb fractures, and tibiofibular fractures require vigilance.

Abbreviations

SSI: Surgical site infection; S. aureus: Staphylococcus aureus; S. epidermis: Staphylococcus epidermis; S. hemolyticus: Streptococcus hemolyticus; AB: Acinetobacter baumannii (AB); PA: Pseudomonas aeruginosa; KP: Klebsiella pneumoniae; E.coli: Escherichia coli.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Zhejiang Provincial People's Hospital.

Consent for publication:

Written informed consent was obtained from each patients'parents for the publication of this report and the accompanying images.

Availability of data and materials:

The datasets generated and/or analyzed during the current study are not publicly but are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

Xinjin Chen designed the study. Yu Tong, Yin Zhang, Wei Zhang and Zheping Hong collected relevant data. Junchao Luo analyzed and interpreted the data. Junchao Luo and Xinjin Chen wrote the manuscript. Qiong Zhang and Qing Bi approved the final version of the manuscript.

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Figures

Figure 1

The distribution of microorganisms in limb fractures. We defined microorganism with frequencies less than 6 times as rare microorganisms.

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