Microbiology Characteristics and Risk Factors of Surgical Site Infection in Limb Fractures: a Single-center Retrospective Study

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Research article

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Abstract

Background: Limb fractures were becoming more common, and internal fixation increased the risk of surgical site infection. The purpose of this study was to identify risk factors for surgical site infection and the factors that affected the microbiological characteristics.

Material and methods: Data from patients with limb fractures who received internal fixation between January 2010 and January 2020 were included. Univariate and multivariate logistic analyses were performed to determine independent risk factors.

Results: A total of 4479 patients were identified and 187 (4.18%) patients developed surgical site infections (SSI). Staphylococcus aureus (25.1%) was the most common bacteria, followed by Coagulase negative Staphylococcus (18.8%) and Acinetobacter baumannii (12.0%). Multiple regression analysis revealed that low total protein (OR, 4.066; 95% CI, 1.217-13.583) and high white blood cell count (OR, 3.133; 95% CI, 1.291-7.605) were risk factors for gram-negative bacteria infection. Five risk factors were identified to be independently associated with the development of SSIs, including current smoking (OR, 2.923; 95% CI, 1.294-6.599), high-energy injury (OR, 2.816; 95% CI, 1.368-5.799), femoral fracture, tibia and fibula fracture, vascular injury at the fracture site (OR, 10.284; 95% CI, 2.506-42.199), skin contusin at the fracture site (OR, 3.348; 95% CI, 1.304-8.574), hypohemoglobin (OR, 2.991; 95% CI, 1.422-6.292).

Conclusion: Preoperative preventative measures should be taken in patients at high risk to reduce the incidence of SSIs.

Introduction:

Limb bones are more vulnerable to the violence that causes fractures than axial and skull bones. With the development of transportation and the rise of fierce confrontational movements, the incidence and number of limb fractures is increasing. Although conservative treatment can achieve beneficial results for some stable fractures, open reduction and internal fixation is still the most common treatment.

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. [1] Previous studies have identified some risk factors associated with SSIs after surgical treatment of limb fracture, including greater BMI, rheumatoid arthritis, diabetes mellitus, smoking, open fracture, lower leg fracture, delayed operation, prolonged operative time, low albumin and high blood glucose. [2-8] However, few studies have focused on the factors affecting the microbiological characteristics of SSIs of limb fractures. Furthermore, most of these studies have focused on specific fracture types.

The purpose of this study is to describe the overall microbiological characteristics and incidence of SSIs after limb fracture. The second is to identify the factors that affect the microbiological characteristics. Risk factors for surgical site infection are identified.

Methods:
We performed a retrospective case-control study at a grade III level A hospital (Zhejiang Provincial People's Hospital) after obtaining approval from the institutional review board. From January 2010 to January 2020, all patients with limb fractures treated with open reduction and internal fixation were included in the study. Fracture sites included humerus, ulnar and radius, femur, patella, tibia and fibula, and foot. The exclusion criteria were pathologic fractures and treatment other than internal fixation (external fixation, conservative treatment, manual reduction, traction, amputation).

We accessed the database of hospital and screened out 4479 patients meeting the inclusion. Next, four physicians recorded data of each patients, including gender, age, BMI (kg/m²), comorbidities (hypertension, heart disease, diabetes mellitus, chronic obstructive pulmonary disease, liver disease, renal disease, cerebrovascular disease), rheumatic diseases, smoking status, alcohol intake, previous surgery at any site, history of allergy to medications/food, mechanism (low or high energy injury), fracture site, nerve injury at the fracture site, vascular injury at the fracture site, skin contusion at the fracture site, fracture type (open or closed), American Society of Anesthesiologists Index (ASA), preoperative hospital stay, hospital stay, intraoperative blood transfusion, postoperative drainage, infections, infecting microorganisms and drug sensitivity test results. Preoperative laboratory indexes included white blood cell (WBC) count, neutrophils (NEUT) count, lymphocyte (LYM) count, red blood cell (RBC), Hemoglobin (HGB) level, platelet (PLT) count, blood glucose, serum total protein (TP) level, albumin (ALB) level, globulin (GLOB) count, and A/G value (albumin/globulin). Among patients who did not develop infection, preoperative laboratory indexes were included only in patients within the last 2 years.

We defined low energy injury as simple falls from standing height, and high energy injury as traffic accidents, falls from a substantial height, and sporting activity. SSI was defined according to a standard 2008 Centers for Disease Control and Prevention (CDC) definition. [9] 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 SSIs were analyzed using a univariate and multivariate models. The t-test was used to compare the differences of continuous variables, while the chi-square test was used for rate and categorical variables. Variables 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:

During the study period, a total of 4842 patients with limb fractures underwent surgery, and 363 patients were excluded under our strict criteria, with the remaining 4479 patients included for data analysis. There were 2592 males and 1887 females, with a mean age of 51.3 years (SD, 18.7;Range, 1-104). 1351 (30.2%) of limb fractures were high energy injuries, and 317 (7.1%) were open fractures. The most common fractures were in the tibia and fibula (1156, 25.8%) and ulna and radius (1039, 23.2%). This was followed by femoral fractures (909, 20.3%). The number of fractures of humerus, foot and patella were 554 (12.4%), 423 (9.4%) and 398 (8.9%), respectively. The average preoperative hospital stay was 6.1 days (SD, 6.5;The Range of 0-61). 1087
were operated on within 2 days, 2393 on days 3 to 7, and the remaining 999 on more than 7 days after admission. [Table 1]

**Microbiology:**

The microorganism most frequently isolated from infected surgical wounds was *Staphylococcus aureus* (S. aureus) (25.1%). This was followed by *Coagulase negative Staphylococcus* (CONS) (18.8%). The next were *Acinetobacter baumannii* (AB) (12.0%) and *Pseudomonas aeruginosa* (PA) (8.3%) respectively. Distribution of microorganism according to fracture site also was showed in Table 2.

Methicillin-resistant S. aureus (MRSA) prevalence was 81.3% (39 strains). The prevalence of multidrug-resistant (MDR) AB and MDR PA were 78.3% (19 strains) and 6.3% (1 strains) respectively. *Klebsiella pneumoniae* (KP) Producing ESBL prevalence was 36.4% (4 strains).

In univariate analysis, 7 variables were found to be significantly associated with gram-positive or gram-negative bacterial infection. (P < 0.05) They included Vascular injury at the fracture site, fracture type, ASA index, preoperative stay, WBC, NEUT, blood glucose and TP. 13 variables were found to be approximately associated with gram-positive or gram-negative bacterial infection., including age, BMI, cerebrovascular disease, fracture site, nerve injury at the fracture site, skin contusion at the fracture site, postoperative drainage use, LYM, HGB, ALB, GLOB. (P < 0.2, P < 0.05) [Table 3]

Multiple categorical variables included age, BMI, fracture site, preoperative stay, LYN, and PLT. In the multivariate regression analysis, the age group < 50 years was taken as dummy variable. BMI, LYM and PLT were used as dummy variables in the normal group. Foot fracture was used as dummy variable for fracture site. The preoperative stay group ≤ 2 days was used as dummy variable. Analysis results show that the significant risk factors for gram-negative bacterial infection occurrence are lower TP (odds ratio [OR], 4.066; 95% CI, 1.217-13.583) and higher WBC (OR, 3.133; 95% CI, 1.291-7.605).

**Risk factors:**

Univariate analysis revealed that the significant risk factors for development of SSIs after internal fixation of limb fractures were heart disease, diabetes mellitus, rheumatic diseases, current smoking, alcohol abuse, mechanism, fracture site, nerve injury at the fracture site, vascular injury at the fracture site, skin contusion at the fracture site, fracture type, ASA index, preoperative stay, intraoperative blood transfusion, postoperative drainage use, WBC, NEUT, LYM, RBC, HGB, PLT, blood glucose, TP and ALB. (P < 0.05) The approximately risk factors were BMI, chronic obstructive pulmonary disease, cerebrovascular disease and GLOB. (P < 0.2, P < 0.05)

In the multivariate logistic regression model, the processing of multiple classification variables was the same as the previous part and the results had been detailed in Table 4. Our results show that the significant risk factors for SSI occurrence were current smoking, high-energy injury, femoral fracture, tibia and fibula fracture, vascular injury at the fracture site, skin contusion at the fracture site, hypohemoglobin. [Table 4]

**Discussion:**
Consistent with previous studies, gram-positive bacteria (including S. aureus and CONS) are the greatest threat to orthopedic SSI. [10-12] The bacteria is continuously colonized the anterior nasal passage in about 20% of the population and intermittently colonize up to 60%. [13, 14] Recent 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 SSIs. Accordingly, we support the view of screening patients for S. aureus colonization before major surgery and intervening if necessary. Gram-negative bacteria infection is more common in developing countries. [17] In our study, AB, PA and KP account for a high proportion of gram-negative bacteria. AB and PA mainly attack patients with low immunity and are difficult to treat because they are often MDR.

Active infection surveillance plays an important role in reducing the risk of SSIs, but this mechanism is not well developed in developing countries. [10] Cefuroxime is currently the antibiotic used for perioperative antibiotic prophylaxis in orthopedics, however, recent studies have shown that strains isolated from SSIs are generally resistant to cefuroxime. Although approximately half of the strains in our study are not tested for sensitivity to cefuroxime, up to 90.9% of the strains tested are resistant to cefuroxime, which supports the view that existing preoperative antibiotic prophylaxis strategies may need to be reconsidered. [19] Compared with other studies, MDR-AB, MDR-PA, and KP producing EBSL account for a lower rate in our study. [20] Cumulative unit-based antibiogram reflects the antibiotic sensitivity patterns of strains isolated from SSIs occurring in this unit, thus providing guidance for empirical therapy. [Table 5]

Many studies have found an association between low serum protein levels and an increased risk of SSIs. [21-23] Serum protein levels reflects the nutritional status of the patient and illness severity during acute-phase reacting. Similarly, WBC also reflects the severity of patient's stress response. Yaning Sun and his colleagues found that increased NEUT in the acute phase-were associated with an increased risk of SSIs. [24] H Claude Sagi and his colleagues found that increased WBC before surgery increased the risk of surgical site infection for pelvic and acetabular fractures. [25] For the first time, we found an association between low TP and increased WBC and an increased risk of gram-negative bacterial infection after internal fixation of fractures. Dong Hyun Oh and his colleagues found that hypoalbuminemia is a risk factor for AB infection after lung transplantation. [26] In our study, open fracture account for a high proportion. Open fractures increase the risk of wound contamination, and the Eastern Association for the Surgery of Trauma (EAST) recommends that perioperative prevention of type III open fractures with antibiotics that cover gram-negative bacteria. [27] Low TP and high WBC generally predict a more severe traumatic shock and intense stress response, which may account for the increased risk of gram negative bacteria infection.

The incidence of SSIs after open reduction and internal fixation of limb fractures varies greatly with study design, surgical site, and study subjects. Małgorzata Kopahe et al reviewed 2659 patients with non-spinal fracture who received open reduction and internal fixation and found a 1.39% occurrence of SSIs. [28] Devon J. Ryan et al performed a retrospective study of 22578 patients with upper limb fractures and found that the incidence of SSIs was 0.79%. [29] Chenni Ji et al reported that the combined postoperative SSIs incidence rate was 3.76% in a retrospective study including 692 patients who received internal fixation for femoral fractures. [30] Prakash Doshi et al found a 3.6% prevalence of SSIs in a prospective study of tibial fractures. [31] Yaning Sun et al reviewed 1543 patients with ankle fracture undergoing internal fixation and found a 4.37%
occurrence of SSIs. [24] In this study, the SSIs rate after limb fractures was 4.18%, which was in the range of previously reported data.

The association between smoking and an increased risk of SSIs has been reported many times. [32-34] Smoking is known to increase the risk of SSIs by causing local tissue hypoxia and inflammation through microvasospasm and systemic inflammation. As a modifiable risk factor, it is necessary to discuss the importance of smoking cessation with patients during the perioperative period.

High energy injuries usually mean more serious injuries and a risk of potential wound contamination. This has been confirmation in other studies. [24, 35] In our study, vascular injury at the fracture site is also identified as an independent risk factor for SSIs. Damage to deep blood vessels also means more severe injuries. Besides, the local tissue hypoxia and the accumulation of harmful metabolites further reduce the immune defense function of the tissue.

The role of skin contusion in the development of SSIs following orthopaedic surgeries has been demonstrated in many previous studies. [36] When planning a surgical approach, orthopedic surgeons usually choose to avoid skin tissue that has been contused. Compared with skin tissue which is simply punctured, skin tissue with contusion has poor ability to heal, which increases the risk of SSIs.

We identify femoral fractures and tibia and fibula fractures as independent risk factors for surgical site infection of limb fractures, consistent with the infection rates we have observed in the previous literature. [29, 30, 37] The location of femoral fracture is deep, and the trauma caused to the body during the reduction of fracture is large, which may be the reason for the higher risk of infection after femoral fracture surgery. Besides, relatively longer bed time is usually required after femoral fracture surgery, which also increase the risk of SSI. The tibia and fibula have less soft tissue covering, which increases the risk of contamination of the fracture. Meanwhile, it also means relatively poor ability of surgical incision healing.

Low HGB level is identified as an independent risk factor for SSIs in our study. Jia-Ming Liu et al reviewed 2715 patients who underwent posterior lumbar surgery and found that low HGB level is risk factor of SSIs. [38] Chenni Ji et al performed a retrospective study of 692 patients with femoral neck fractures and also found that low HGB level is risk factor of SSIs. [30] These results indicate the importance of low hemoglobin levels in the development of SSIs. In high-risk patients with multiple risk factors, preoperative mandatory optimization should be considered.

Proper placement of drainage tubes helps to reduce the risk of SSIs. For patients with less exudation, some physicians may choose not to place a drainage tube. This explains the high percentage of drainage tube placement in infected patients.

The advantages of this study included large simple size of patients, a relatively long follow-up period and the numerous variables included for data analysis. However, the inherent defects of retrospective study affected the accuracy of data collection. There were some variables that could not be abstracted from database, such as operation time, surgeon level, etc., which have been reported as risk factors in past studies. Furthermore, some patients who had developed an SSI might go to another hospital for treatment, thus lead to underestimate incidence of SSIs.
Conclusion:

The current retrospective single-center study found that the infection rate of SSIs after limb fracture was 4.18%. S. aureus was the most common bacteria, followed by CONS and AB. The significant risk factors for gram-negative bacteria infection were lower TP and higher WBC. Five risk factors were identified to be independently associated with the development of SSIs, including current smoking, high-energy injury, femoral fracture, tibia and fibula fracture, vascular injury at the fracture site, skin contusin at the fracture site, hypohemoglobin. Identification of these risk factors can facilitate risk benefit analysis of preoperative prophylaxis and improve preoperative counseling.

Abbreviations:

SSI: Surgical site infection; S. aureus: Staphylococcus aureus; CONS: Coagulase negative Staphylococcus ; AB: Acinetobacter baumannii; PA: Pseudomonas aeruginosa; KP: Klebsiella pneumoniae; E.coil: Escherichia coli; MDR: Multidrug-resistant; ASA: American Society of Anesthesiologists Index; WBC: White blood cell; NEUT: Neutrophils; LYM: lymphocyte; RBC: Red blood cell; HGB: Hemoglobin; PLT: Platelet; TP: Total protein; ALB: Albumin; GLOB: Globulin; A/G: Albumin/Globulin.

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. Yin Zhang, Yu Tong, Wei Zhang, Senbo Zhu and Lichen Ji 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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References:

1. Ban KA, Minei JP, Laronga C et al. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. *J Am Coll Surg.* 2017;224(1):59-74
2. Reese SM, Knepper B, Young HL, Mauffrey C. Development of a surgical site infection prediction model in orthopaedic trauma: The Denver Health Model. *Injury.* 2017;48(12):2699-2704
3. Lu K, Zhang J, Cheng J et al. Incidence and risk factors for surgical site infection after open reduction and internal fixation of intra-articular fractures of distal femur: A multicentre study. *Int Wound J.* 2019;16(2):473-478
4. Zhao K, Zhang J, Li J et al. Incidence and risk factors of surgical site infection after intertrochanteric fracture surgery: A prospective cohort study. *Int Wound J.* 2020;17(6):1871-1880
5. Xu H, Yu L, Li Y, Gong Z. Prolonged surgical duration, higher body mass index and current smoking increases risk of surgical site infection after intra-articular fracture of distal femur. *Anz J Surg.* 2019;89(6):723-728
6. Richards JE, Kauffmann RM, Zuckerman SL, Obremskey WT, May AK. Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. *J Bone Joint Surg Am.* 2012;94(13):1181-6
7. den Broeder AA, Creemers MC, Fransen J et al. Risk factors for surgical site infections and other complications in elective surgery in patients with rheumatoid arthritis with special attention for anti-tumor necrosis factor: a large retrospective study. *J Rheumatol.* 2007;34(4):689-95
8. Su J, Cao X. Risk factors of wound infection after open reduction and internal fixation of calcaneal fractures. *Medicine (Baltimore).* 2017;96(44):e8411
9. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control.* 2008;36(5):309-32
10. Pawłowska I, Ziółkowski G, Wójkowska-Mach J, Bielecki T. Can surgical site infections be controlled through microbiological surveillance? A three-year laboratory-based surveillance at an orthopaedic unit, retrospective observatory study. *Int Orthop.* 2019;43(9):2009-2016
11. Shah MQ, Zardad MS, Khan A et al. Surgical Site Infection In Orthopaedic Implants And Its Common Bacteria With Their Sensitivities To Antibiotics, In Open Reduction Internal Fixation. *J Ayub Med Coll Abbottabad.* 2017;29(1):50-53
12. Montalvo RN, Natoli RM, O’Hara NN et al. Variations in the Organisms Causing Deep Surgical Site Infections in Fracture Patients at a Level I Trauma Center (2006-2015). *J Orthop Trauma.* 2018;32(12):e475-e481
13. Mehraj J, Witte W, Akmatov MK et al. Epidemiology of Staphylococcus aureus Nasal Carriage Patterns in the Community. *Curr Top Microbiol Immunol*. 2016;398:55-87

14. Laux C, Peschel A, Krismer B. Staphylococcus aureus Colonization of the Human Nose and Interaction with Other Microbiome Members. *Microbiol Spectr*. 2019;7(2)

15. Tsang S, McHugh MP, Guerendiain D et al. Evaluation of Staphylococcus aureus eradication therapy in orthopaedic surgery. *J Med Microbiol*. 2018;67(6):893-901

16. Sporer SM, Rogers T, Abella L. Methicillin-Resistant and Methicillin-Sensitive Staphylococcus aureus Screening and Decolonization to Reduce Surgical Site Infection in Elective Total Joint Arthroplasty. *J Arthroplasty*. 2016;31(9 Suppl):144-7

17. Tuon FF, Cieslinski J, Ono A et al. Microbiological profile and susceptibility pattern of surgical site infections related to orthopaedic trauma. *Int Orthop*. 2019;43(6):1309-1313

18. Helal S, El AM, Ghaith D, Rabeea S. The Role of MDR-Acinetobacter baumannii in Orthopedic Surgical Site Infections. *Surg Infect (Larchmt)*. 2015;16(5):518-22

19. Xu SG, Mao ZG, Liu BS, Zhu HH, Pan HL. Evaluating the use of antibiotic prophylaxis during open reduction and internal fixation surgery in patients at low risk of surgical site infection. *Injury*. 2015;46(2):184-8

20. Tucaliuc D, Alexa O, Tuchiluş CG et al. ANTIBIOTIC RESISTANCE SPECTRUM OF NON FERMENTING GRAM NEGATIVE BACILLI ISOLATED IN THE ORTHOPEDIC TRAUMATOLOGY CLINIC OF "SF. SPIRIDON" CLINICAL EMERGENCY HOSPITAL IAŞI. *Rev Med Chir Soc Med Nat Iasi*. 2015;119(2):536-43

21. Yuwen P, Chen W, Lv H et al. Albumin and surgical site infection risk in orthopaedics: a meta-analysis. *Bmc Surg*. 2017;17(1):7

22. Bai Y, Zhang X, Tian Y, Tian D, Zhang B. Incidence of surgical-site infection following open reduction and internal fixation of a distal femur fracture: An observational case-control study. *Medicine (Baltimore)*. 2019;98(7):e14547

23. Ren M, Liang W, Wu Z, Zhao H, Wang J. Risk factors of surgical site infection in geriatric orthopedic surgery: A retrospective multicenter cohort study. *Geriatr Gerontol Int*. 2019;19(3):213-217

24. Sun Y, Wang H, Tang Y et al. Incidence and risk factors for surgical site infection after open reduction and internal fixation of ankle fracture: A retrospective multicenter study. *Medicine (Baltimore)*. 2018;97(7):e9901

25. Sagi HC, Dziadosz D, Mir H, Virani N, Olson C. Obesity, leukocytosis, embolization, and injury severity increase the risk for deep postoperative wound infection after pelvic and acetabular surgery. *J Orthop Trauma*. 2013;27(1):6-10

26. Oh DH, Kim YC, Kim EJ et al. Multidrug-resistant Acinetobacter baumannii infection in lung transplant recipients: risk factors and prognosis. *Infect Dis (Lond)*. 2019;51(7):493-501

27. Garner MR, Sethuraman SA, Schade MA, Boateng H. Antibiotic Prophylaxis in Open Fractures: Evidence, Evolving Issues, and Recommendations. *J Am Acad Orthop Surg*. 2020;28(8):309-315

28. Kolpa M, Slowik R, Wałaszek M et al. Multimodal strategy in surgical site infections control and prevention in orthopaedic patients - a 10-year retrospective observational study at a Polish hospital. *Antimicrob Resist Infect Control*. 2020;9(1):20
29. Ryan DJ, Minhas SV, Konda S, Catalano LW. Surgical Site Infection After Open Upper Extremity Fracture and the Effect of Urgent Operative Intervention. *J Orthop Trauma*. 2020;34(5):258-262

30. Ji C, Zhu Y, Liu S et al. Incidence and risk of surgical site infection after adult femoral neck fractures treated by surgery: A retrospective case-control study. *Medicine (Baltimore)*. 2019;98(11):e14882

31. Doshi P, Gopalan H, Sprague S et al. Incidence of infection following internal fixation of open and closed tibia fractures in India (INFINITI): a multi-centre observational cohort study. *BMC Musculoskelet Disord*. 2017;18(1):156

32. Jildeh TR, Okoroha KR, Marshall NE et al. Infection and Rerupture After Surgical Repair of Achilles Tendons. *Orthop J Sports Med*. 2018;6(5):2325967118774302

33. Ryan DJ, Minhas SV, Konda S, Catalano LW. Surgical Site Infection After Open Upper Extremity Fracture and the Effect of Urgent Operative Intervention. *J Orthop Trauma*. 2020;34(5):258-262

34. Fisichella L, Fenga D, Rosa MA. Surgical Site Infection In Orthopaedic Surgery: Correlation Between Age, Diabetes, Smoke And Surgical Risk. *Folia Med (Plovdiv)*. 2014;56(4):259-63

35. Wang H, Pei H, Chen M, Wang H. Incidence and predictors of surgical site infection after ORIF in calcaneus fractures, a retrospective cohort study. *J Orthop Surg Res*. 2018;13(1):293

36. Zalavras CG. Prevention of Infection in Open Fractures. *Infect Dis Clin North Am*. 2017;31(2):339-352

37. Shao J, Chang H, Zhu Y et al. Incidence and risk factors for surgical site infection after open reduction and internal fixation of tibial plateau fracture: A systematic review and meta-analysis. *Int J Surg*. 2017;41:176-182

38. Liu JM, Deng HL, Chen XY et al. Risk Factors for Surgical Site Infection After Posterior Lumbar Spinal Surgery. *Spine (Phila Pa 1976)*. 2018;43(10):732-737

**Tables:**
Table 1.
Association between potential risk factors and postoperative SSI in patients with limb fractures undergoing internal fixation surgery.

| Variables | Number (%) of patients without SSI (n = 4292) | Number (%) of patients with SSI (n = 187) | P |
|-----------|-----------------------------------------------|---------------------------------------------|---|
| Gender (male) | 2464 (57.4%) | 128 (68.4%) | 0.003 |
| Age, y | 51.3±18.7 | 51.0±18.3 | 0.604 |
| <50 | 2080 (48.4%) | 87 (46.5%) | 0.604 |
| 50-69 | 1520 (35.4%) | 72 (38.5%) | 0.388 |
| ≥70 | 692 (16.1%) | 28 (14.9%) | 0.675 |
| BMI | 23.7±3.9 | 24.21±3.87 | 0.260 |
| Reference (<24.0) | 2519 (58.69%) | 102 (54.55%) | 0.855 |
| Overweight (24-27.9) | 1213 (28.26%) | 54 (28.88%) | 0.488 |
| Obesity (28-31.9) | 416 (9.69%) | 21 (10.23%) | 0.143 |
| Morbid obesity (>32) | 144 (3.35%) | 10 (5.35%) | 0.143 |
| Hypertension | 666 (15.5%) | 29 (15.6%) | 0.997 |
| Heart disease | 12 (0.2%) | 3 (1.6%) | 0.001 |
| Diabetes mellitus | 274 (6.3%) | 24 (12.8%) | 0.001 |
| Chronic obstructive pulmonary disease | 43 (1.0%) | 4 (2.1%) | 0.095 |
| Liver disease | 60 (1.3%) | 2 (1.1%) | 0.798 |
| Renal disease | 35 (0.8%) | 1 (0.5%) | 0.738 |
| Cerebrovascular disease | 244 (5.6%) | 5 (2.7%) | 0.121 |
| Rheumatic diseases | 619 (14.4%) | 4 (2.1%) | 0.001 |
| Current smoking | 567 (13.2%) | 49 (26.2%) | 0.001 |
| Alcohol abuse | 347 (8.9%) | 36 (19.3%) | 0.001 |
| History of previous operation at any site | 347 (8.1%) | 3 (1.6%) | 0.002 |
| History of allergy to medications/food | 42 (1.0%) | 3 (1.6%) | 0.500 |
| Mechanism | 1236 (28.8%) | 115 (61.5%) | 0.001 |
| Fracture site | | | |
| Diagnosis                                      | Cases | Controls | p-value |
|-----------------------------------------------|-------|----------|---------|
| Humerus                                       | 544 (12.6%) | 10 (5.3%) | 0.003   |
| Ulna and Radius                               | 1030 (23.9%) | 9 (4.8%) | 0.001   |
| Femoral                                       | 866 (20.1%) | 43 (22.9%) | 0.348   |
| Patella                                       | 384 (8.9%) | 14 (7.4%) | 0.492   |
| Tibia and Fibula                              | 1062 (24.7%) | 94 (50.2%) | 0.001   |
| Foot                                          | 406 (9.4%) | 17 (9.0%) | 0.866   |
| Nerve injury at the fracture site             | 249 (5.8%) | 29 (15.5%) | 0.001   |
| Vascular injury at the fracture site          | 27 (0.6%) | 29 (15.51%) | 0.001 |
| Skin contusion at the fracture site           | 163 (3.7%) | 33 (17.6%) | 0.001   |
| Fracture type (open)                          | 228 (5.3%) | 89 (47.5%) | 0.001   |
| American Society of Anesthesiologists Index   |       |          |         |
| I-II                                          | 4060 (94.6%) | 157 (84.0%) | 0.001   |
| III-IV                                        | 232 (5.4%) | 30 (16.0%) | 0.001   |
| Preoperative stay, d                          | 5.9±6.3 | 7.3±7.7 |         |
| 0-2                                           | 1020 (23.8%) | 63 (33.7%) | 0.001   |
| 3-7                                           | 2340 (54.5%) | 57 (30.5%) | 0.001   |
| 7                                             | 932 (21.7%) | 67 (35.8%) | 0.001   |
| Intraoperative blood transfusion              | 73 (1.7%) | 10 (5.3%) | 0.031   |
| Postoperative drainage use                    | 1154 (26.9%) | 81 (43.3%) | 0.001   |
| WBC, 10^9/L                                   | 8.39±3.71 | 10.47±5.27 |       |
| 9.5                                           | 175 (29.3%) | 90 (48.1%) | 0.001   |
| NEUT, 10^9/L                                  | 6.19±3.59 | 8.52±4.85 |       |
| 6.3                                           | 240 (40.3%) | 117 (62.6%) | 0.001   |
|                 | Reference Range | Number    | Percentage | p Value |
|----------------|-----------------|-----------|------------|---------|
| **LYM, 10^9/L**|                 |           |            |         |
|                | 1.59±0.56       | 1.44±1.09 |            |         |
| **References (1.1-3.2)** |           |           |            |         |
|                | 407 (68.6%)     | 99 (52.9%)|            | 0.001   |
| **<1.1**       |                 |           |            |         |
|                | 169 (28.5%)     | 76 (40.6%)|            | 0.002   |
| **>3.2**       |                 |           |            |         |
|                | 17 (2.9%)       | 12 (6.4%) |            | 0.025   |
| **RBC, 10^{12}/L** |           |           |            |         |
|                | 4.13±0.74       | 3.40±0.87 |            |         |
| **< lower limit** |           |           |            |         |
|                | 182 (30.7%)     | 128 (68.4%)|            | 0.001   |
| **HGB, g/L**   |                 |           |            |         |
|                | 124.94±21.82    | 101.18±27.46|           |         |
| **< lower limit** |           |           |            |         |
|                | 188 (31.5%)     | 113 (60.4%)|            | 0.001   |
| **PLT**        |                 |           |            |         |
|                | 213.22±92.41    | 180.46±107.76|           |         |
| **References (100-300)** |           |           |            |         |
|                | 511 (85.6%)     | 114 (61.0%)|            | 0.001   |
| **<100**       |                 |           |            |         |
|                | 59 (9.9%)       | 55 (29.4%) |            | 0.001   |
| **>300**       |                 |           |            |         |
|                | 27 (4.5%)       | 18 (9.6%)  |            | 0.009   |
| **Blood glucose (abnormal)** |           |           |            |         |
|                | 176 (29.8%)     | 88 (47.1%) |            | 0.001   |
| **TP, g/L**    |                 |           |            |         |
|                | 64.26±8.46      | 53.12±13.08|           |         |
| **<60**        |                 |           |            |         |
|                | 288 (48.3%)     | 144 (77.0%)|            | 0.001   |
| **ALB, g/L**   |                 |           |            |         |
|                | 38.07±5.37      | 31.15±7.74 |            |         |
| **<35**        |                 |           |            |         |
|                | 374 (62.8%)     | 163 (87.2%)|            | 0.001   |
| **GLOB, g/L**  |                 |           |            |         |
|                | 26.19±5.36      | 22.00±6.67 |            |         |
| **<30**        |                 |           |            |         |
|                | 99 (16.6%)      | 20 (10.7%) |            | 0.050   |
Table 2.
Distribution of bacteria according to fracture site.

| Bacteria                          | Case n (%) | MDR n (%) | Humerus (RV) | Ulna and Radius (RV) | Femoral (RV) | Patella (RV) | Tibia and Fibula (RV) | Foot (RV) | P     |
|----------------------------------|------------|-----------|--------------|----------------------|--------------|--------------|------------------------|-----------|-------|
| Staphylococcus aureus            | 48 (25.1)  | 39 (81.3) | 0.40         | 0.22                 | 0.16         | 0.29         | 0.29                   | 0.23      | 0.596 |
| Coagulase negative Staphylococcus | 36 (18.8)  |           | 0.20         | 0.11                 | 0.23         | 0.29         | 0.16                   | 0.24      | 0.781 |
| Enterococcus faecalis            | 6 (3.1)    |           | 0.00         | 0.00                 | 0.00         | 0.00         | 0.63                   | 0.00      | 0.293 |
| Acinetobacter baumannii          | 23 (12.0)  | 18 (78.3) | 0.00         | 0.00                 | 0.19         | 0.07         | 0.15                   | 0.00      | 0.182 |
| Pseudomonas aeruginosa           | 16 (8.3)   | 1 (6.3)   | 0.10         | 0.11                 | 0.12         | 0.00         | 0.09                   | 0.06      | 0.837 |
| Klebsiella pneumoniae            | 11 (5.7)   | 4 (36.4)  | 0.10         | 0.11                 | 0.07         | 0.07         | 0.04                   | 0.06      | 0.931 |
| Proteus mirabilis                | 8 (4.1)    |           | 0.10         | 0.00                 | 0.12         | 0.00         | 0.02                   | 0.00      | 0.097 |

*MDR Multidrug-resistant: Include methicillin-resistant Staphylococcus aureus (MRSA), multidrug-resistant Acinetobacter baumannii, multidrug-resistant Pseudomonas aeruginosa and Klebsiella pneumoniae producing extended-spectrum beta-lactamases (ESBL);

RV Relative Value: The number of patients with infection at this site / The number of fractures at this site.
Table 3. Association between potential risk factors and microbiological characteristics in patients with limb fractures undergoing internal fixation surgery.

| Variables                              | Number (%) of patients with gram-positive bacteria infection (n=109) | Number (%) of patients with gram-negative bacteria infection (n=78) | P     |
|----------------------------------------|---------------------------------------------------------------|-----------------------------------------------------------------|-------|
| Gender (male)                          | 72 (66.1%)                                                    | 56 (71.1%)                                                      | 0.408 |
| Age, y                                 | 52.0±18.9                                                     | 49.6±17.4                                                       |       |
| <50                                    | 48 (44.0%)                                                    | 39 (50.0%)                                                      | 0.420 |
| 50-69                                   | 41 (37.6%)                                                    | 31 (39.7%)                                                      | 0.768 |
| ≥70                                    | 20 (18.3%)                                                    | 8 (10.2%)                                                       | 0.126 |
| BMI                                    | 23.6±3.8                                                      | 23.7±3.4                                                        |       |
| Reference (<24.0)                      | 60 (55.0%)                                                    | 42 (53.85%)                                                     | 0.871 |
| Overweight (24-27.9)                   | 33 (30.3%)                                                    | 21 (26.92%)                                                     | 0.618 |
| Obesity (28-31.9)                      | 9 (8.3%)                                                      | 12 (15.38%)                                                     | 0.128 |
| Morbid obesity (>32)                   | 7 (6.4%)                                                      | 3 (3.85%)                                                       | 0.440 |
| Hypertension                           | 19 (17.4%)                                                    | 10 (12.8%)                                                      | 0.393 |
| Heart disease                          | 2 (1.8%)                                                      | 1 (1.3%)                                                        | 0.804 |
| Diabetes mellitus                      | 14 (12.8%)                                                    | 10 (21.8%)                                                      | 0.996 |
| Chronic obstructive pulmonary disease   | 2 (1.8%)                                                      | 2 (2.6%)                                                        | 0.693 |
| Liver disease                          | 2 (1.8%)                                                      | 0 (0.0%)                                                        | 0.245 |
| Renal disease                          | 1 (0.9%)                                                      | 0 (0.0%)                                                        | 0.412 |
| Cerebrovascular disease                | 1 (0.9%)                                                      | 4 (5.1%)                                                        | 0.067 |
| Rheumatic diseases                     | 3 (2.8%)                                                      | 1 (1.3%)                                                        | 0.529 |
| Current smoking                        | 29 (26.7%)                                                    | 20 (25.6%)                                                      | 0.899 |
| Alcohol abuse                          | 21 (19.3%)                                                    | 15 (19.2%)                                                      | 0.913 |
| History of previous operation at any site | 1 (0.9%)                                                    | 2 (2.6%)                                                        | 0.380 |
| History of allergy to medications/food | 1 (0.9%)                                                      | 2 (2.6%)                                                        | 0.380 |
| Mechanism                              | 64 (58.7%)                                                    | 51 (65.4%)                                                      | 0.400 |
| Fracture site                          | 6 (5.5%)                                                      | 4 (5.1%)                                                        | 0.910 |
| Category                                      | Cases | %    | Reference Cases | %    | P-value |
|-----------------------------------------------|-------|------|-----------------|------|---------|
| Ulna and Radius                               | 3     | 2.8% | 6               | 7.6% | 0.120   |
| Femoral                                       | 21    | 19.3%| 22              | 28.2%| 0.152   |
| Patella                                       | 9     | 8.3% | 5               | 6.4% | 0.636   |
| Tibia and Fibula                              | 58    | 53.2%| 36              | 46.1%| 0.341   |
| Foot                                          | 12    | 11.0%| 5               | 6.4% | 0.281   |
| Nerve injury at the fracture site             | 13    | 11.9%| 16              | 20.5%| 0.111   |
| Vascular injury at the fracture site          | 11    | 10.1%| 18              | 23.0%| 0.015   |
| Skin contusion in the fracture site           | 15    | 13.8%| 18              | 23.0%| 0.100   |
| Fracture type (open)                          | 44    | 40.4%| 45              | 57.6%| 0.019   |
| American Society of Anesthesiologists Index  |       |      |                 |      |         |
| I-II                                          | 98    | 89.9%| 59              | 75.6%| 0.009   |
| III-IV                                       | 11    | 10.1%| 19              | 24.4%| 0.009   |
| Preoperative stay, d                          | 7.9±7.6|      | 6.5±8.0         |      |         |
| 0-2                                          | 30    | 27.5%| 33              | 42.3%| 0.035   |
| 3-7                                          | 39    | 35.8%| 18              | 23.1%| 0.063   |
| ≥7                                           | 40    | 36.7%| 27              | 34.6%| 0.770   |
| Intraoperative blood transfusion              | 3     | 2.8% | 7               | 9.0% | 0.234   |
| Postoperative drainage use                    | 41    | 37.6%| 40              | 51.3%| 0.199   |
| WBC, $10^9$/L                                 | 8.88±3.78|     | 12.60±6.23      |      |         |
| ≤9.5                                         | 39    | 35.8%| 51              | 65.4%| 0.004   |
| NEUT, $10^9$/L                                | 7.08±3.53|    | 10.49±5.70      |      |         |
| ≤6.3                                         | 59    | 54.1%| 58              | 74.4%| 0.038   |
| LYM, $10^9$/L                                 | 1.37±0.93|     | 1.53±1.28       |      |         |
| References (1.1-3.2)                          | 61    | 56.0%| 38              | 48.7%| 0.328   |
| <1.1                                         | 44    | 40.4%| 32              | 41.05%| 0.928  |
| >3.2                                         | 4     | 3.7% | 8               | 10.3%| 0.070   |
| Parameter                     | Value 1          | Value 2          | p-value |
|-------------------------------|------------------|------------------|---------|
| RBC, $10^{12}$/L              | 3.47±0.92        | 3.30±0.80        | 0.834   |
| < lower limit                 | 74 (67.9%)       | 54 (69.2%)       |         |
| HGB, g/L                      | 103.18±30.42     | 98.44±22.84      |         |
| < lower limit                 | 55 (50.5%)       | 58 (74.4%)       | 0.142   |
| PLT                           | 178.73±104.41    | 182.84±113.40    |         |
| References (100-300)          | 67 (61.5%)       | 47 (60.3%)       | 0.867   |
| <100                          | 31 (28.4%)       | 24 (30.8%)       | 0.730   |
| >300                          | 11 (10.1%)       | 7 (9.0%)         | 0.798   |
| Blood glucose (abnormal)      | 40 (36.7%)       | 48 (61.5%)       | 0.019   |
| TP, g/L                       | 56.04±12.23      | 48.95±13.25      |         |
| <60                           | 75 (68.8%)       | 69 (88.5%)       | 0.032   |
| ALB, g/L                      | 32.65±7.54       | 29.01±7.59       |         |
| <35                           | 91 (83.5%)       | 72 (92.3%)       | 0.159   |
| GLOB, g/L                     | 23.44±6.31       | 19.94±6.70       |         |
| >30                           | 15 (13.8%)       | 4 (5.1%)         | 0.103   |
Table 4.
Multivariate analysis of factors associated with surgical site infection after open reduction and internal fixation of limb fractures.

| Variables                                      | Exp (B) | 95% CI (lower limit) | 95% CI (upper limit) | P    |
|------------------------------------------------|---------|----------------------|----------------------|------|
| Current smoking                                | 2.923   | 1.294                | 6.599                | 0.010|
| Mechanism                                      | 2.816   | 1.368                | 5.799                | 0.005|
| Fracture site                                  |         |                      |                      |      |
| Humerus                                        | 0.566   | 0.084                | 3.818                | 0.559|
| Ulna and Radius                                | 0.324   | 0.031                | 3.425                | 0.349|
| Femoral                                        | 12.478  | 2.635                | 59.093               | 0.001|
| Patella                                        | 1.897   | 0.259                | 13.882               | 0.529|
| Tibia and Fibula                               | 8.445   | 2.245                | 31.772               | 0.002|
| Vascular injury at the fracture site           | 10.284  | 2.506                | 42.199               | 0.001|
| Skin contusion at the fracture site            | 3.348   | 1.304                | 8.574                | 0.012|
| Postoperative drainage use                     | 2.818   | 1.374                | 5.776                | 0.005|
| Hemoglobin level                               | 2.991   | 1.422                | 6.292                | 0.004|

Table 5.
The cumulative antibiogram report.

| Bacteria                                      | %I     | Ciprofl oxacin | Cotrimoxazole | Ceftazidime | Amikacin |
|------------------------------------------------|--------|----------------|---------------|-------------|----------|
|                                                | %S     | IF             | %S            | IF          | %S       | IF      |
| Staphylococcus aureus                         | 10.1   | 94.1           | 9.50          | 100         | 10.10    | N/A     | N/A     |
| Methicillin-resistant Staphylococcus aureus    | 15.4   | 22.7           | 3.50          | 86.2        | 13.27    | N/A     | N/A     |
| Coagulase-negative staphylococcus             | 18.8   | 27.2           | 5.11          | 66.6        | 12.52    | N/A     | N/A     |
| Acinetobacter baumannii                       | 12.0   | 17.6           | 2.11          | 23.5        | 2.82     | 9.1     | 1.09    | 50.0    | 6.00    |
| Pseudomonas aeruginosa                        | 8.3    | 85.7           | 7.11          | 8.3         | 0.69     | 86.7    | 7.20    | 93.8    | 7.79    |
| Klebsiella pneumoniae                         | 5.7    | 50.0           | 2.85          | 44.4        | 2.53     | 33.3    | 1.90    | 77.8    | 4.43    |
| Proteus mirabilis                             | 4.1    | 62.5           | 2.56          | 37.5        | 1.54     | 100     | 4.10    | 100     | 4.10    |
| Percentage of overall activity                | 51.40  | 52.36          | 57.28         | 80.40       |          |         |         |         |
*N/A not available; %I percentage frequency of isolation; %S percentage sensitivity of pathogen to antibiotic; IF antimicrobial impact factor: the likelihood that a pathogen would be sensitive to an antimicrobial drug, (%I×%S)/100