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Original Article

Etiological spectrum and treatment outcome of wound infection in patients with open tibia and fibula fractures

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Abstract: Objective: To explore the etiology of wound infections in patients with open tibia and fibula fractures and the treatment effects. Methods: In this retrospective study, a total of 76 patients with open tibia and fibula fractures were included in this research. These patients were divided into the control group (n=38) and the observation group (n=38) according to the treatment methods for wound infection. The distribution and drug resistance of pathogenic bacteria in wound infections were analyzed. Clinical effects, time for body temperature returning to normal, time for disappearance of exudates, time for clearance of pathogenic bacteria, recovery effects and patients' satisfaction rate were also compared between two groups. Results: A total of 152 strains of pathogenic bacteria were separated. The main pathogenic bacterium was Acinetobacter baumannii, accounting for 30.92% (47/152). Pathogenic bacteria were demonstrated to be highly sensitive to vancomycin and imipenem. The proportion of wound healing by first intention and the Johner-Wruhs scores in observation group were significantly higher than those in control group, while recurrent infection rate, the time to restore normal body temperature, the time for exudates to disappear, the time to remove pathogenic bacteria, hospital stays and VAS scores in observation group were obviously shorter or lower than those in control group (all $P<0.05$). Moreover, the satisfaction rate of patients in the observation group was significantly higher than that in the control group ($P<0.05$). Conclusion: Understanding pathogenic characteristics and drug resistance of wound infection in patients with open tibia and fibula fractures is helpful to subsequent treatment. Comprehensive control measures should be taken to decrease incidence of wound infection.

Keywords: Open tibia and fibula fractures, wound infection, pathogenic bacteria, treatment

Introduction

Open tibia and fibula fracture is a common type of fracture, which is characterized by local swelling and pain in the fracture area, displacement, angulation, and/or deformity, etc. [1]. It was reported that patients with open tibia and fibula fractures were usually accompanied by different degrees of trauma and soft tissue damage, easily resulting in the occurrence of infection [2, 3]. In critically ill patients, complications such as tissue ischemia, hypoxic necrosis and muscle spasms may occur [4]. The primary treatment for open tibia and fibula fractures caused by high-energy injury includes rigid fixation, anatomical reduction and so on [5]. Clinically, surgical treatment basically refers to the internal fixation with steel plates. However, due to improper operation approach or timing, and severe damage to the soft tissues around the fracture area, a wide range of complications including bone non-union, infectious osteomyelitis, implant exposure, soft tissue defect, and wound infection may occur [6, 7], which could affect the wound healing and even lead to serious dysfunction, thus increase the pain of the patients and pose a serious threat to the life of the patients [8].

Wound infection is the most common complication of open fracture, which not only causes severe symptoms such as bone exposure and ischemic necrosis, but also directly affects the treatment effect and functional recovery. Previous studies showed that if postoperative wound infection in elderly patients with open fracture was not well prevented and treated, it would influence the effect of fracture repair and lead to sepsis [9, 10]. Moreover, some studies reported that the median costs per patient were significantly higher in infected patients than those not, mainly due to the prolonged length of hospital stay [11]. Another study revealed that the rate of amputation after recurrent infection was about 3%-5% [12]. Whereas there is still a lack of consensus on the guidelines for the treatment of fracture-related infections, and there are few reports on the etiological characteristics and treatment methods of postoperative wound infection in patients with open tibia and fibula fractures. Therefore, finding an optimal therapeutic strategy is a challenge for surgeons. In this context, we observed the etiology of postoperative wound infection and compared the outcomes after comprehensive treatment in contrast with conventional antibiotic drugs. The results of this study may provide some clinical evidence for management of postoperative wound infection in patients with open fractures.

Materials and methods

Subjects

A total of 76 patients with open tibia and fibula fractures admitted to the Orthopedics Department in Hangzhou Fuyang Hospital of TCM from January 2017 to December 2021 were retrospectively included in this study. Inclusion criteria: ① Patients with postoperative infection of their wound confirmed by laboratory examination and microbiological detection. ② Patients with complete medical records. ③ Patients who had internal fracture fixation. ④ Patients who had good compliance and were able to cooperate with this research. Exclusion criteria: ① Patients with infected fracture wounds before operation. ② Patients with wound fat liquefaction following operation. ③ Patients who had external fixation, bone traction, surgical debridement or amputation. ④ Patients who rejected internal fracture fixation. This research was approved by the Ethics Committee of Hangzhou Fuyang Hospital of TCM Orthopedics and Traumatology (Approval No.2016-127) and all the included patients or their families signed the informed consent. All of the operations were performed by the same medical team. The enrolled patients were assigned into two groups with 38 patients in each group. The infected wounds in the control group were treated with sensitive antibiotic drugs, while those in the observation group were treated with comprehensive treatments.

Specimen collection

The wound secretions from patients were collected under sterile conditions and placed in sterile tubes. The VITEK-2 Compact automatic bacterial identification and drug sensitivity analysis system (BioMérieux Company, France) were used for specimen isolation. The drug sensitivity test was conducted using the agar dilution method, followed by bacteriological culture, with reference to the standards proposed by the Clinical and Laboratory Standards Institute (CLSI) in 2007.

Treatment methods

In the control group, the postoperative infection in patients was treated with sensitive antibiotic drugs. The dressing was changed 1-2 times per day to ensure that the incision was clean and tidy. Nutritional support was also provided at the same time.

The infected wounds in the observation group underwent comprehensive treatment. Any purulent secretions or inflamed biofilm that formed on the surface of the steel plate were removed and the internal fixation was retained. The collected specimens were used for the drug sensitivity test and bacterial culture. Then, a cotton pad soaked with hydrogen peroxide was applied to the infected wound for 5 minutes. After cleaning with saline solution, the wound was covered with a pad soaked in 1% povidone-iodine for 3 minutes. Next, percutaneous catheters were placed at both ends of the incision to reach the implant. The drainage tube was kept in below the position of the distal incision, while the irrigation tube was placed in the position above the proximal incision. It was ensured that these two drainage tubes were unblocked. The wound healing by first intention was treated with demixing suture and full thickness suture, followed by covering with povidone-iodine gauze. The postoperative incision was washed until there was no tissue debris or blood clots and the drainage liquid was clear. Functional exercise including contraction exercises of quadriceps femoris muscle, and flexion

Table 1. General information of patients

Parameters	Total (N=76)	Control group (N=38)	Observation group (N=38)	χ^2/t value	*P* value
Male/Female	58/18	30/8	28/10	0.291	0.590
Age (years)	59.88±6.10	60.32±6.41	59.43±6.32	0.610	0.544
BMI (kg/m^2)	23.94±0.90	23.83±0.88	24.15±0.93	1.541	0.128
Infection time (h)	5.47±1.08	5.51±1.11	5.43±1.02	0.327	0.745
Causes of injuries (n)				0.906	0.636
Traffic injury	31	14	17		
Crush injury	19	10	9		
Falling injury	26	15	11		
Underlying disease (n)				0.068	0.967
Great vessels breakage	6	3	3		
Hypertension	7	4	3		
Diabetes	11	6	5		

and extension exercises of malleolus were conducted after improved infection.

Outcome observations

The primary observation indicators included distribution of pathogenic bacteria in the infected wound, drug resistance of pathogenic bacteria and clinical effects. The infection was considered to be curable according to the following standards: ① No drainage fluid or negative bacterial culture of secretions for 3 d. ② Fresh color in the incision without being swollen. ③ Normal blood work. Clinical effects were compared between the two groups, which were composed of wound healing by first intention, wound healing by second intention and recurrent infection.

The second observation indicators included time to restore normal body temperature, time for exudates to disappear, time to remove pathogenic bacteria, recovery effects and satisfaction rate of patients. The recovery effects were evaluated in terms of hospital stays, Visual analogue scores (VAS) and Johner-Wruhs scores.

VAS was applied for assessing the pain degree of patients in both groups [13]. The scale ranges from 0-10 with 0 representing no pain and 10 representing severe pain.

Johner-Wruhs score was used to evaluate the recovery of limb function [14], which covers 4 items of operation time, knee range of motion, ankle range of motion, and healing time. The scale ranges from 0 to 100. Higher scores indicated better effects.

The patients' satisfaction rate on treatment plans was compared between two groups [15]. The satisfaction was surveyed by an anonymous questionnaire sheet with a total score of 100 points. The judgment criteria were as follows: scores more than 90 points suggested excellent satisfaction; scores between 70 and 90 points suggested general satisfaction; less than 70 points indicated dissatisfaction. The satisfaction rate was calculated in the following formula: Satisfaction rate = (the cases of patients with excellent satisfaction + the cases of patients with general satisfaction)/total number of patients × 100%.

Statistical analysis

The observed data in this research were analyzed using SPSS software 22.0 and GraphPad Prism 8.0.1. Measurement data were expressed as mean ± standard deviation. The independent t-tests were used for intergroup comparison. Count data were expressed as percentages or cases, and χ^2 tests were used for intergroup comparison. $P<0.05$ suggested statistical differences.

Results

Basic data

The general information of 76 eligible patients in this study are presented in **Table 1**. No significant differences in gender, age, BMI, cause of injury, time of infection and underlying diseases were found between the control group and observation group (all $P>0.05$), indicating comparability between the two groups.

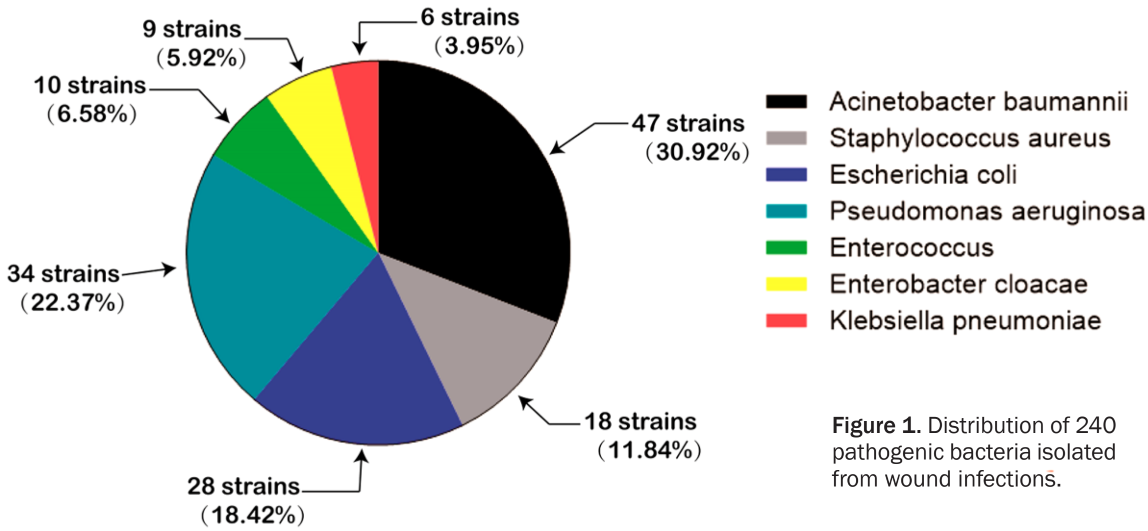

Figure 1. Distribution of 240 pathogenic bacteria isolated from wound infections.

Table 2. Drug resistance of pathogens to various antibiotics

Antibacterial agents	Acinetobacter baumannii (n=47)		Escherichia coli (n=28)		Pseudomonas aeruginosa (n=34)	
	Strains	Drug resistance rate	Strains	Drug resistance rate	Strains	Drug resistance rate
Vancomycin	0	0.00	0	0.00	0	0.00
Mezlocillin	36	76.59	14	50.00	20	58.82
Penicillin	44	93.62	13	46.43	28	82.35
Azlocillin	37	78.72	19	67.86	21	61.76
Levofloxacin	20	42.55	15	53.57	19	55.88
Imipenem	1	2.13	0	0.00	1	2.94
Ceftriaxone	18	38.29	20	71.43	22	64.71
Amikacin	33	70.21	22	78.57	27	79.41
Ciprofloxacin	39	82.98	25	89.29	30	88.24

Distribution of pathogenic bacteria in early wound infections

As shown in **Figure 1**, in the 76 patients with early wound infections following internal fixation of tibiofibular fractures, a total of 152 strains of pathogenic bacteria were isolated, mainly including Acinetobacter baumannii (30.92%, 47/152), Staphylococcus aureus (11.84%, 18/152), Escherichia coli (18.42%, 28/152), Pseudomonas aeruginosa (22.37%, 34/152), Enterococcus (6.58%, 10/152), Enterobacter cloacae (5.92%, 9/152), and Klebsiella pneumoniae (3.95%, 6/152), respectively.

Drug resistance analysis

As shown in **Table 2**, the drug resistance rate of Acinetobacter baumannii to Vancomycin, Imipenem, Ceftriaxone, Levofloxacin, Amikacin, Mezlocillin, Azlocillin, Ciprofloxacin and Penicillin was 0.0%, 2.13%, 38.29%, 42.55%, 70.21%, 76.59%, 78.72%, 82.98% and 93.62%, respectively. The drug resistance rate of Escherichia coli to Vancomycin, Imipenem, Penicillin, Mezlocillin, Levofloxacin, Azlocillin, Ceftriaxone, Amikacin, Ciprofloxacin and was 0.0%, 0.0%, 46.43%, 50.00%, 53.57%, 67.86%, 71.43%, 78.57% and 89.29%, respectively. The drug resistance rate of Pseudomonas aeruginosa to Vancomycin, Imipenem, Levofloxacin, Mezlocillin, Azlocillin, Ceftriaxone, Amikacin, Penicillin and Ciprofloxacin was 0.0%, 2.94%, 55.88%, 58.82%, 61.76%, 64.71%, 79.41%, 82.35% and 88.24%, respectively. Acinetobacter baumannii, Escherichia coli and Pseudomonas aeruginosa were highly sensitive to Vancomycin and Imipenem.

Table 3. Analysis of clinical efficacy in the two groups of patients

Groups	Wound healing by first intention	Wound healing by second intention	Recurrent infection
Control group (n=38)	17 (44.74)	21 (55.26)	4 (10.53)
Observation group (n=38)	26 (68.42)	12 (31.58)	0 (0.00)
χ^2 value	4.338		4.222
P value	0.037		0.039

Table 4. Comparison of clinical indicators between the two groups

Groups	Time to restore normal body temperature (d)	Time for exudates to disappear (d)	Time to remove pathogenic bacteria (d)
Observation group (n=38)	10.02±1.21	15.98±1.76	18.15±1.74
Control group (n=38)	14.04±1.46	18.97±1.85	22.35±2.41
t value	13.069	7.218	8.710
P value	<0.001	<0.001	<0.001

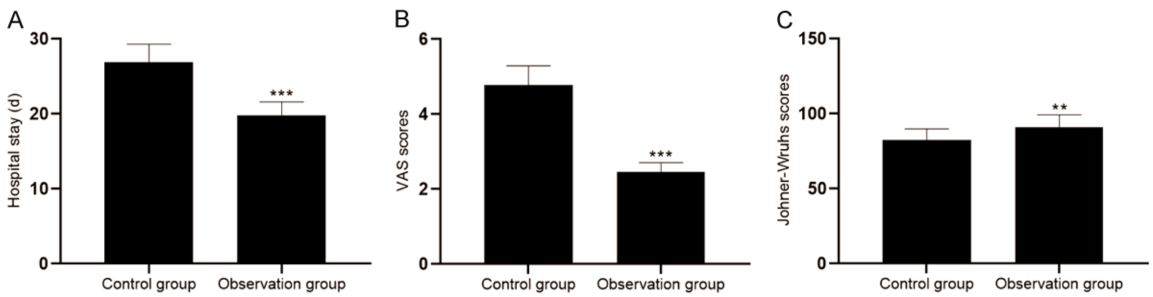

Figure 2. Comparison of recovery between two groups. A: Hospital stay. B: VAS scores. C: Johner-Wruhs scores. Compared with control group, ***P<0.001, **P<0.01. VAS, Visual analogue scores.

Comparison of clinical effects between two groups

As shown in **Table 3**, the proportion of wound healing by first intention and second intention in the control group was 44.74% and 55.26%, respectively; while those in the observation group were 68.42% and 31.58%, respectively (all P<0.05). Moreover, the recurrent infection rate in the observation group was significantly lower than that in the control group (0 vs 15.3%, P=0.039).

Comparison of time to restore normal body temperature, time for exudates to disappear, time to remove pathogenic bacteria

As shown in **Table 4**, the time to restore normal body temperature, time for exudates to disappear, time to remove pathogenic bacteria in the observation group were 10.02±1.21 d, 15.98±1.76 d and 18.15±1.74 d, respectively, while those in the control group were 14.04±1.46 d, 18.97±1.85 d and 22.35±2.41 d, respectively (all P<0.001).

Comparison of hospital stay, VAS and Johner-Wruhs scores

As shown in **Figure 2**, the length of hospital stay in the observation group was 19.84±1.76 d, which was significantly shorter than that in the control group 26.87±2.45 d (P<0.001). Compared with control group (4.78±0.51), VAS scores in the observation group (2.46±0.25) were significantly decreased (P<0.001). In additional, the Johner-Wruhs score in the observation group was significantly higher than that in the control group (82.42±7.53 vs 91.22±8.14, P<0.01).

Comparison of satisfaction

As shown in **Table 5**, in the control group there were 11 patients with excellent satisfaction, 17 patients with general satisfaction and 10

Table 5. Comparison of satisfaction between the two groups

Group	Excellent satisfaction	General Satisfaction	Dissatisfaction	Rate of satisfaction
Control group	11	17	10	28 (73.68%)
Observation group	24	10	4	34 (89.47%)
χ^2 value				7.957
P value				0.019

patients with dissatisfaction, while there were 24 cases with excellent satisfaction, 10 patients with general satisfaction and 4 patients with dissatisfaction in the observation group. The satisfaction rate in the observation group was significantly higher than that in the control group (P=0.019).

Discussion

Wound infection following open fractures of the tibia and fibula is a serious complication, which can affect the postoperative recovery of patients. It can easily lead to chronic osteomyelitis and infectious nonunion if not treated in time, which not only increases the suffering of patients and the difficulty of treatment, but also results in the possibility of amputation. Thus, clinical workers need to pay close attention to wound infection [16, 17].

Multivariate analysis showed that the severity of bone injury was a risk factor for infection [18]. Many studies reported that debridement during the period from trauma occurrence to hospital admission should not be neglected [19]. The longer the debridement interval was, the more likely to develop infection, and longer treatment interval was considered as a risk factor for wound infection in patients [20]. At present, antibiotic drugs are widely used in clinical practice. However, drug resistance is usually developed due to the wide varieties, excessive change frequency and irrational application of antibiotics, resulting in dysbacteriosis and further aggravating the infection [21]. It was reported that the probability of infection in patients who received combined antibiotics was about three times that in patients not receiving combined antibiotics, indicating that unreasonable application of antibiotics was a risk factor for infection in patients [22-24]. Clinically, wound infection after internal fracture fixation is treated with antibacterial drugs such as third-generation cephalosporin and carbapenems.

In this study, 152 strains of pathogenic bacteria were isolated from wound secretions in 76 patients who underwent internal fixation of open tibia and fibula fractures. The pathogenic bacteria were mainly Acinetobacter baumannii, Escherichia coli, and Pseudomonas aeruginosa, among which Pseudomonas aeruginosa were ubiquitous in nature and considered as the major bacteria in hospital infection. In terms of drug resistance, most of the patients had a high drug resistance rate. This study showed that most pathogens exhibited drug resistance except to imipenem and vancomycin. The results of this study also suggested that wound infection was associated with serious trauma, severe impairment of organ function and poor constitution, which was in accordance with previous studies [9]. Another study reported that the bacterial biofilm on the surface of biological material or the body mucosa contributed to the secretion of complexes such as proteoglycan matrixs and fibrous proteins, which promoted the adhesion of bacteria to each other. It was necessary to strengthen anti-infective treatment following internal fractures fixation [25, 26]. As we can see, this study provided an etiological basis and a good guide for the precise selection of antibiotics for these patients with wound infection after internal fixation of tibia and fibula fractures.

Conventional antibiotics are usually used to treat wound infections after internal fixation of tibia and fibula fractures. However, many studies revealed that patients treated with antibiotics generally had some shortcomings such as longer time to restore normal body temperature, and longer time to clear exudates and pathogenic bacteria and hospital stay [27, 28]. In this study, a combination of antibiotics, debridement, irrigation and drainage was implemented. The drainage tube was inserted beneath the incision as low as possible, which promoted the discharge of necrotic material and enhanced the healing. Some studies reported that the combined treatment of antibiotics and debridement, irrigation and drainage could decrease the length of hospital stay and increase the cure rate in patients with early wound infection after internal fixation of tibia and fibula fractures [29-31]. Gauze soaked with povidone-iodine was frequently applied to wipe off the biofilm on the wound surface. The results of this study also showed that in patients who received the combined treatment, the proportion of wound healing by the first intention was significantly higher than those who received routine antibacterial drugs. Moreover, there was no recurrence of infection in the observation group, and the VAS score in the observation group was obviously lower than that in the control group. Besides, the time to restore normal body temperature, the time to clear exudates and pathogenic bacteria and hospital stay were significantly shorter, while Johner-Wruhs scores and patients' satisfactory rate in the observation group were significantly higher than those in the control group. This may be because the repeated application of povidone-iodine showed long-lasting sterilization activity and was not affected by the purulence, which was helpful to tissue dehydration, inhibition of granulation tissue growth, blood oozing and fluid oozing, and ultimately promoted wound healing [32, 33].

There are still some limitations in this study. Firstly, this is a retrospective study with limited information which may cause certain selection bias. Second, the sample size was small, which means this research was underpowered. Third, there is no comparative analysis of clinical outcomes among different types of fractures and the follow-up period was short. In order to provide more scientific results, we will perform a multi-centered, randomized control, and long-time follow up study.

In summary, there is a wide distribution of pathogenic bacteria in infected wounds after internal fixation of tibia and fibula fractures. In order to reduce the drug-resistance, broad-spectrum antibiotics should be used with caution. Comprehensive measures, which have better advantages in the term of clinical effects, recovery effects and the satisfactory of patients, could be considered in the treatment of wound infection following internal fixation of tibia and fibula fractures.

Disclosure of conflict of interest

None.

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