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Antibiotic Prophylaxis in Bacterial Infection of Type IIIA Open Fracture of Tibial Shaft With or Without Fibula Fracture

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Abstract

Background: A major purpose of treating open fractures is the prevention of wound infection. Infection, as a major complication associated with open fractures, may lead to limb loss, sepsis, and even death. In this study, we survey factors affecting infection.
Objectives: In this study, we survey factors affecting infection.
Patients and Methods: The study population consisted of all patients with type IIIA gastilo open fractures of tibial shaft, with or without fibula fracture (caused by trauma). After wound irrigation, debridement, and wound swab sampling for microbial culture, all patients received prophylactic antibiotic regimens in fitting with their wound class. No topical antibiotics were used with a 6-month follow-up for any symptom of osteomyelitis.
Results: Considering the occurrence of one case of infection, the infection rate was calculated (1.89%). Given the low prevalence rate of infection, it was difficult to evaluate the effect of different antibiotic regimens on the prevention of infection (in terms of regimen duration). As such, no specific regimen was preferred. The results of statistical analysis did not show any significant difference between one-day application of antibiotic prophylaxis and two or three days consumption of antibiotic prophylaxis.
Conclusions: According to the results of this study, one-day administration of antibiotics as prophylaxis (first generation of cephalosporins) was sufficient for the prevention of infection after orthopedic surgery in all patients except in patient with risk factors such as diabetes or immune deficiency, when the administration of prophylactic antibiotic lasts for 3 days.

Keywords: Antibiotic Prophylaxis, Fracture of Tibial Shaft, Bacterial Infection

1. Background

A main objective in the treatment of open fractures is the prevention of wound infection. Infection, as a major complication pursuing open fractures, may lead to limb loss, sepsis, and death. Despite advances in the treatment of open fractures, delayed infection ensues in 2 - 25% of such fractures.

The treatment of these fractures poses a tremendous challenge to surgeons (1, 2). Open fractures are often categorized according to Gustilo-Anderson classification, which has prognostic and treatment values (3). Wound infection rate depends on the extent of damage to soft tissue and the class of open wound. The rate of open fractures for different grades are as follows: grade I, 0 - 2%, grade II, 2 - 7%, grade III, 10 - 25%, grade IIIA, 7%, grade IIIB, 10 - 50%, and grade IIIC, 25 - 50%.

Positive effects of antibiotics have been well documented in patients with open fractures (2). According to a study by Gustilo and Anderson, open fractures require emergency treatment like adequate debridement and irrigation of the wound. Also, antibiotics should be administered before and during surgery. If the wound is primarily closed, the administration of antibiotics is halted on the third day after surgery, but if the wound is secondarily closed, the administration continues for another three days after the procedure (1).

Treatment with broad-spectrum antibiotics after injury and invasive surgical debridement reduces the incidence of infection in open fractures of the limbs, with significant improvement in functional results of open fractures. If physicians can diagnose the infected wounds, they will be able to make suitable interventions to prevent infectious complications (4).

However, sufficient knowledge of wound contamination and microbial flora is required to prescribe an effective and reasonable antibiotic regimen (5). There is no consensus about the length of antibiotic therapy in open fracture with the predictions ranging between 1 and 10 days (2). Two out of three cases of deep wound infection, including an implanted biomaterial, are monomicrobial, with most isolated bacteria in osteomyelitis and orthopedic device-related infections being related to *Staphylococcus aureus* and *Staphylococcus epidermidis* (1).

Microbial flora of open fractures has changed since late 1970's. Coagulase-positive *Staphylococcus* was the dominant pathogen in the 70's and early 80's, but penicillin-resistant coagulase-positive bacteria, gram-negative bacteria and a combination of organisms (which require a combination of antibiotic treatments) can also cause infections (2). In the study of Gustilo and Anderson in 1976, the dominant organisms were coagulase-positive *Staphylococcus*, *Klebsiella*, *Enterobacter*, *Escherichia coli*, *Proteus*, and coagulase-negative *Staphylococcus* (6, 7).

Sufficient knowledge of pathogens-causing wound infection in open fractures is required for rational prescription of antibiotics and infection prevention. Since the bacteriological pattern of infecting organisms changes over time, further studies are required to determine and prevent unsuitable or excessive diets and antimicrobial resistance (8).

Approximately 60% of open fractures are contaminated at the time of injury. In many studies, a variety of methods have been used to identify wounds, as the potential infection sites in early stages. However, there is no consensus about the need for multiple sequential cultures and sensitivity evaluation of open fracture wounds; therefore, more comprehensive studies are required in this field (6, 9).

Some researchers still doubt the infection prediction, based on pre and post-debridement cultures, but they acknowledge higher prognostic values of post-debridement cultures. Others maintain that both smear and culture can be of predictive value in the management of traumatic wounds, if taken at early stages, or when the microbial load exceeds 105 CFU/g in skin tissue, or when there is a microbial load in the muscles.

Some researchers have not reported any quantitative association between the presentation time of fracture (until debridement) and microbial load, while others have suggested the higher predictive value of post-debridement quantitative bacterial for infection (10).

In 35% of initial cultures, no organism grew; however, when the culture was positive and the wound was infected, the cultured organism could cause the infection. Other studies found insignificant association between primary bacterial culture and subsequent sepsis (2, 11).

In the past, primary wound culture in open fractures was a common way of identifying infection-causing organism in the early stages thus selecting a suitable antibiotic treatment.

Given the high prevalence and significance of open fracture infections in patients' morbidity and considering the conflicting results regarding the effective factors, causative pathogens, appropriate diagnostic methods, and effective antibiotic regimens (in the treatment of deep and surface infections of the fracture site), it is necessary to conduct comprehensive studies with adequate sample size. In addition, it is essential for medical centers to determine the bacteriological pattern and resistance of effective microbes in causing infection. In fact, it can help prevent infections, improve health outcomes and antibiotic prescriptions, and hinder the occurrence of antibiotic resistance.

2. Objectives

Therefore, we conducted a study on patients with open tibial fractures who had been injured in car accidents. The aim of our study was to evaluate the contributory factors of infection, the importance and value of diagnostic methods like culturing, bacteriological patterns, and microbial resistance in pathogens causing infections. We also assessed the effectiveness of prescribed regimens in preventing infections caused by pathogens.

3. Patients and Methods

This study consisted of all admitted patients with type IIIA open fractures of tibial shaft, with or without fibula fracture (caused by trauma). The subjects had normal immune status and good health before the accident. The subjects were studied in terms of infection frequency and effective pathogen(s) in a 19-month interval from December 2010 to July 2013.

The exclusion criteria were as follows: 1) a history of recent hospitalization, 2) the use of antibiotic treatment, 3) compromised immune system or cancer, 4) treatment with corticosteroids, 5) a history of osteomyelitis, 6) limb amputation, and 7) death due to trauma.

After wound irrigation, debridement, and wound swab sampling for microbial culture, all patients received prophylactic antibiotic regimens based on the wound class in the absence of any topical antibiotics. The wound was immediately bandaged without exerting any pressure. Skeletal fixation and soft tissue repair were implemented in all patients within 72 hours after debridement.

Deep osteomyelitis is defined as the inflammation of bone, bone marrow, and surrounding soft tissues, characterized by ongoing pain, secretion, or swelling accompanied by a significant increase in inflammatory markers [increased body temperature > 38°C and white blood count (WBC) > 12,000], with or without radiological evidence.

The data were collected using checklists that provided the following information: 1) patient's characteristics; 2) type of fracture; 3) site of tibial fracture; 4) interval between fracture and the first evidence of infection; 5) pre-debridement swab culture at the time of admission; 6) post-debridement swab culture; 7) cultured organism in the wound surface swab at the first detection of infection symptoms and before changing antibiotic regimen; 8) wound surface culture of the debrided tissue during surgery; 9) number of debridements before discharge; and 10) length of hospitalization.

The patients were followed up for 6 months after the accident to check any sign of osteomyelitis (patients were assessed on a daily basis during hospitalization and every four weeks after discharge since the day of admission in the clinic), and the data were recorded in the checklists. In case of osteomyelitis or symptoms of infection, culture, antibiogram, and sample biopsy were performed and the results were recorded. Additionally, disc diffusion method was used for organism culture along with antibiogram of aerobic and anaerobic organisms.

In this study, attempts were made to match surgeon-related risk factors for all patients; therefore, all subjects were shaved in the operating room (OR) right before surgery. All patients underwent surgery in two specific ORs. Despite the undesirable condition of air ventilation and the number of people in the OR their impacts on the results were overlooked as they were almost identical for all patients.

Statistical analysis was carried out using SPSS and conventional statistical methods such as frequency tables and graphs. Then, using Chi-square, the existence of any significant relationships between variables was assessed. P value less than 0.05 were considered statistically significant.

4. Results

In total, 103 patients with tibial fractures, with or without fibular fractures, referred to the center in the period between December 2010 and July 2013. Fifty-three patients met the inclusion criteria and were followed up for 6 months after surgery. The mean age of the patients was 65 years. In terms of lymphocyte count, 64% of patients had a total lymphocyte count (TLC) of less than 1500 and suffered from malnutrition (Figure 1).

Thirteen percent of patients with a serum albumin of less than 3.4 g/dL were within the malnutrition range (Figure 2). In terms of transferrin status, none of the patients had transferrin less than 150; therefore, none suffered from malnutrition (Figure 3). Considering the disparity of results in this regard, the nutritional index of the patients was calculated using the following formula:

Nutritional index = [(1.2 × serum Alb) + (0.013 × serum trasnferrin)] - 6.43

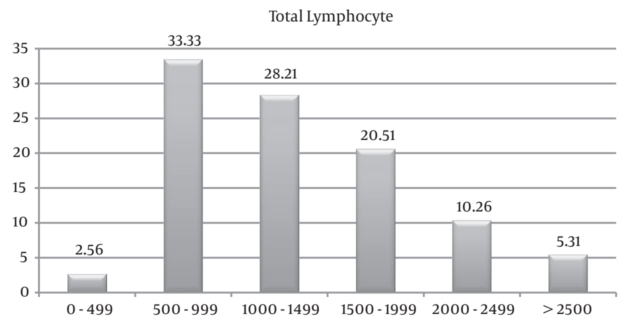

Figure 1. Frequency of Patients in Terms of Lymphocyte Count

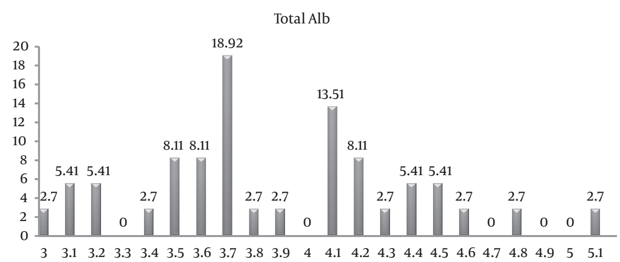

Figure 2. Frequency of Patients in Terms of Total Alb

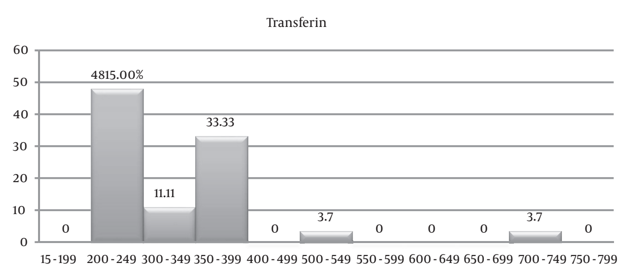

Figure 3. Frequency of Patients in Terms of Transferin Level

The nutritional index of zero or negative was considered as malnutrition. Accordingly, 4% of patients were suffering from malnutrition (Figure 4). Although these patients required nutritional support, as a result of poor resources, they underwent surgery without nutritional status modification. In spite of the high incidence of malnutrition, infection was not observed in any of these patients. Statistically speaking, in terms of infection prevalence, no significant difference was observed between malnourished patients and those with proper nutritional status ($P < 0.05$).

The immune status of the patients, as shown in Figures 5 - 7 was investigated in terms of immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM).

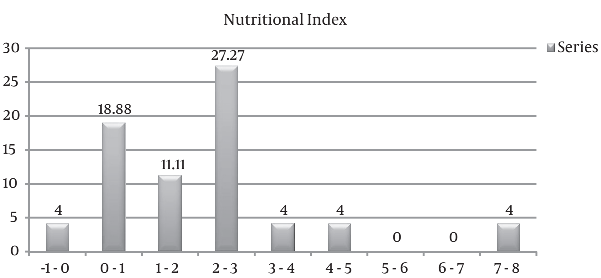

Figure 4. Frequency of Patients in Terms of Nutritional Index

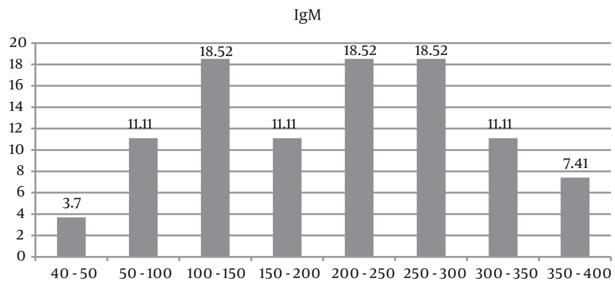

Figure 7. Frequency of Patients in Terms of IgM Level

Normal levels of these variables were defined as IgA < 50 mg/dL, IgG < 500 mg/dL, and IgM < 40 mg/dL, according to Harrison's study. Accordingly, in this study, humoral immunity of all patients was normal. Since normal values of serum immunoglobulins and antibody response are considered as acceptable standards for the normal function of T-cells, it confirms patients' health.

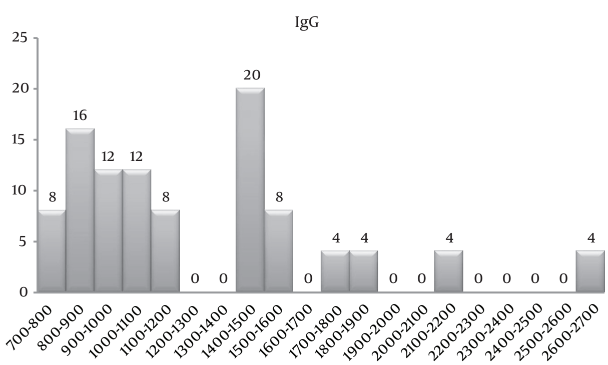

Figure 5. Frequency of IgG Level in Patients

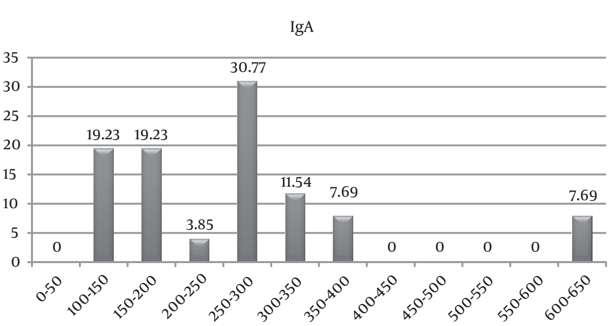

Figure 6. Frequency of Patients in Terms of IgA Level

Another risk factor evaluated in patients was the presence of an infectious focus elsewhere. After gaining a complete history and performing physical examination, if infection was suspected, supplemental tests such as urine analysis, urine culture, and chest X-ray were routinely administered for all patients. In all these evaluations, 26% of patients had urinary tract infections, which were treated prior to the surgery.

Age distribution is shown in Figure 8. According to the results, with increasing age comes increased risk of infection as a result of reduced body's defense mechanism. A comparison of age and lack of TLC showed that 80% of subjects with TLC < 1500 were over 70 years of age, and thus belonged to the high-risk group. On the contrary, in 90% of subjects over 70 years, other risk factors such as urinary tract infection, malnutrition, and diabetes were observed. Accordingly, subjects over 70 years of age were also included in the high-risk group.

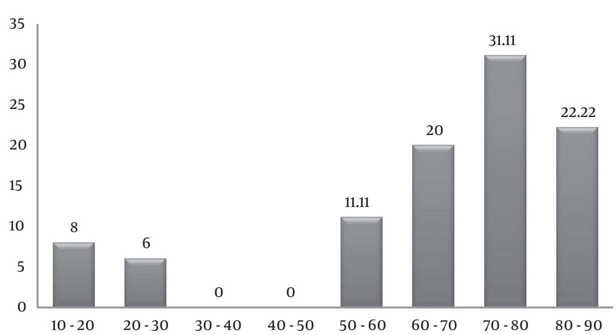

Figure 8. Age Distribution of Patients

In Figure 9, the frequencies of risk factors have been compared. In this study, the most common risk factor was a patient's age, followed by frequency, malnutrition, infection in other parts of the body, diabetes, previous surgery and the use of immunosuppressant respectively.

Comparing the number of patients in different groups and the frequency of infectious and non-infectious cases, we found that only one case had surgical-site infection in

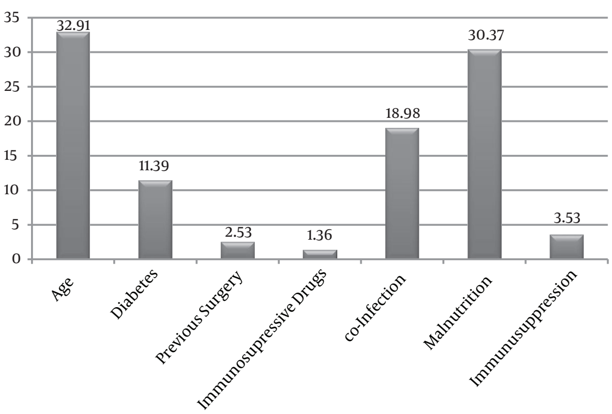

Figure 9. Frequencies of Risk Factors

the high-risk group.

The evaluation of cultures in OR indicated that 15% of surgical instruments were not sterilized before surgery. Also, at the end of surgery, 23% of patients had wound infections, which had mostly caused during surgery (Figure 10).

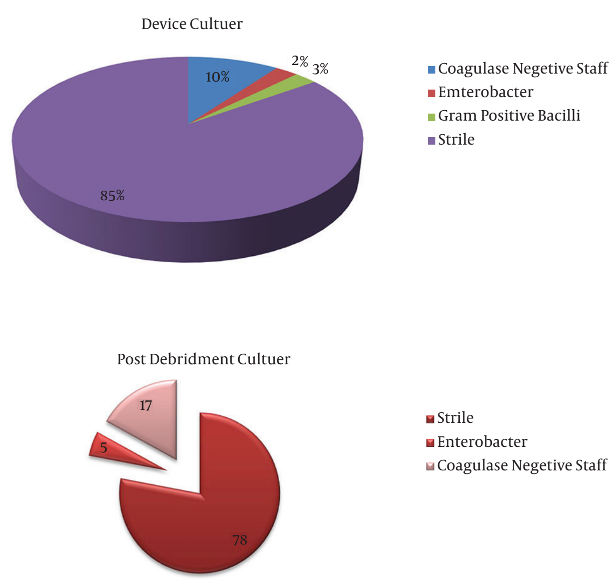

Figure 10. Device Culture and Post Debridement Culture Distribution

In the 6-month follow-up of patients, only one case of infection was observed. In the second culture of this patient's wound secretion, pseudomonas aeruginosa and *Proteus vulgaris* were reported. The patient in the high-risk group had multiple risk factors including old age, urinary tract infection, prolonged hospitalization before surgery (20 days), long duration of surgery (4.5 hours), and kidney failure followed by surgery. In these evaluations, the patient's nutritional status and immune function were normal, and the urinary tract infection was treated prior to the surgery.

Statistical analysis using Chi-square test did not show any significant difference in terms of antibiotic prophylaxis. In other words, it meant that one-day use of antibiotic prophylaxis was not statistically different from two or three days consumption; therefore, one-day use of preventive antibiotics, being as effective as two or three days consumption, would suffice ($P > 0.05$).

5. Discussion

In this study, only one case of infection was observed (infection rate = 1.89%). Considering the low prevalence of infection, it was difficult to evaluate the effect of different antibiotic regimens on the prevention of infection (in terms of regimen duration) therefore no specific regimen was preferred.

On the other hand, the present study did not show any bacterial infections caused by primary open wound, which is in line with the study of Lingaraj et al. (12). They showed that initial flora were not the infecting organisms in the open fracture wounds, and pre-debridement wound cultures was of no value in predicting post-debridement wound infection (12).

However, others have stated that pre-debridement culture is not a good predictor of infected wounds. Faisham et al. (6) studied swabs before, during, and after surgery and analyzed the swab culture of stabilized infection and its sensitivity over a period of 6 months. The microbes grew in 39.3% of pre-debridement swabs, with 75% of them belonging to the group of gram-negative bacteria. Also, 50% of patients with positive postoperative swabs were infected.

Accordingly, the researchers concluded that multiple sequential cultures and their sensitivities were not helpful in the treatment of open fractures (6). The advocates of this theory believe that a possible explanation for the inadequacy of primary wound culture could be the sampling error. Thus at the culturing time, the infection causing pathogen, is not obtained. This is either due to poor sampling or insufficient number of organisms in the sample, which hinders the collection of enough samples.

Another explanation is the antibiotic consumption, which is bactericidal for the organism growth in the primary wound, and therefore leads to the emergence of small quantities of resistant strains bacteria during culturing. Debridement and irrigation change the topical wound ecology, which is necessary for reducing contamination or dead tissues (2, 6, 11).

Finally, it is suggested that infection-causing bacteria might be nosocomial, which are not present at the time of culturing. According to several studies, skin flora are the primary pathogens identified in primary wound cultures; however, such infection could be caused by nosocomial pathogens such as *Pseudomonas aeruginosa*, *Enterobacter cloacae*, and *Enterococcus* (6).

This highlights the importance of undertaking regional studies at different medical centers. In the absence of sufficient scientific findings, two scenarios lie ahead. The first one involves the selection of the cheapest regimen, especially considering the lack of evidence-based studies on the priority of costly regimens, which corresponds to the British legal system. Another scenario is the maximum prescription of available treatments. In the United States, many physicians, who fail to prescribe the maximum available treatments, are accused of inaccuracy (7).

Today, there has been a surge in the prevalence of osteomyelitis as a result of the increasing use of implanted prosthetic devices for the treatment of fractures or (arthritis) (2, 7). The clinical approach to osteomyelitis treatment requires an accurate microbiological diagnosis, which determines the suitable antibacterial regimen to which the organisms are susceptible. The efficacy of treatment depends on a number of factors such as the type of bacteria, the route that bacteria gain entry to the bone, the presence of any orthopedic devices, and the patient's immune response. As a result, treatment often requires a combination of medical and surgical procedures (3, 7, 13).

Tibia is the most common site of open fractures. The treatment of post-traumatic tibial osteomyelitis has been a major clinical challenge for decades (14, 15). Post-traumatic tibial osteomyelitis is caused either by trauma or nosocimial infection during the treatment, which allows the organism to enter the bone, spread in the traumatized tissue, and cause subsequent infection. It should be noted that such an infection is often polymicrobial (16).

The categorization of osteomyelitis is based on May and Cierny-Mader classification, in which the diagnosis is based on the pathogens in blood culture or bone. The appropriate treatment of post-traumatic tibial osteomyelitis, similar to other related conditions, involves adequate drainage, complete debridement, dead spaces removal, stabilization (if necessary), wound protection, and appropriate antibiotic treatment (17, 18).

In addition, osteomyelitis of the tibial diaphysis is a rare but debilitating condition in adults. This condition occurs in patients with complex tibial fractures in which devitalized bone is infected either by a single strain of a virulent organism or multiple organisms. The treatment outcomes depend on the evaluation and treatment of three related factors including bone vitality and stability, virulence and antibiotic susceptibility of the infection- causing organism, and condition of soft tissues (19)

Surgical site infections are not only developed as a result of surgical techniques or bone exposure to infection during surgery (including adequate debridement, wound irrigation, fracture stabilization, and early covering of the soft tissue), but also depend on the pre-operative condition of the patient and the wound, nursing care, nutritional support, hospital hygiene, environmental conditions in hospitals, and microbial flora (8, 11).

In orthopedic surgeries, the use of prosthesis and implants may increase the incidence of infection; therefore, the administration of preventive antibiotic administration, even in clean cases, is recommended. However, considering the low incidence of infection, it is difficult to offer an accurate estimation of the optimal duration of antibiotic administration. In this regard, long-term side effects of antibiotic use (such as microbial resistance and higher health-care costs) should be also taken into account (14, 20).

5.1. Conclusion

According to the results of this study, one-day administration of antibiotics as prophylaxis would suffice for the prevention of infection after orthopedic surgery in all patients ($P < 0.05$). However, due to the high risk of infection, it is recommended to continue intravenous antibiotic administration (without oral antibiotics) in high-risk patients for a maximum of 3 days. In low-risk patients, nonetheless, one day administration would be sufficient (maximum).

Moreover, considering the high prevalence of modifiable risk factors such as malnutrition and infections in other sites, it is recommended to evaluate all patients prior to the surgery to eliminate these risk factors. By comparing the results of pre and post-operative cultures, it can be concluded that a modification of OR conditions is essential. By improving the air ventilation system, limiting the number of people in the OR or reducing OR traffic, implementing precise surgical sterilization, and modifying the performance of radiography in the OR, the incidence of wound contamination can be significantly reduced.

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