

Article

Comparison of Three Antibiotic Prophylaxis Protocols for Preventing Postoperative Infection in Tibial Plateau Fractures

Carolina Montoya-delaTorre ^{1,*}, Ernesto Muñoz-Mahamud ^{1,*} , Jose Alonso Zumbado ¹, Laura Morata ² , Judit Martínez-Peñas ³  and Oscar Ares ¹ 

¹ Department of Orthopedic Surgery and Traumatology, Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain

² Department of Infectious Diseases, Hospital Clinic, University of Barcelona, 08036 Barcelona, Spain

³ Campus Clinic, August Pi i Sunyer, School of Medicine and Health Sciences, University of Barcelona, 08036 Barcelona, Spain; judit.martinez1208@gmail.com

* Correspondence: montoya@clinic.cat (C.M.-d.); emunoz@clinic.cat (E.M.-M.)

Abstract: Background: The aim of this study was to compare the impact of three different types of intraoperative antibiotic prophylaxis on the risk of postoperative surgical site infection (SSI). Material and Methods: Single-center retrospective cohort study. Patients who underwent surgery for osteosynthesis of a tibial plateau fracture (January 2009–November 2018) in Hospital Clinic i Provincial de Barcelona were included. Three types of prophylaxis during the study period were used: group A (cefuroxime single-dose treatment), group B (meropenem + teicoplanin), and group C (ceftriaxone + teicoplanin). Demographics, co-morbidity, type of fracture, need for external fixation, microbiology data, surgical time, and outcome were recorded. Failure was defined as the need for reintervention due to postoperative surgical site infection. Results: From a total of 148 patients included, 20 cases developed SSI, 8 from group A, 8 from group B, and 4 from group C. Higher ASA scores, Schatzker II classification, need for external fixation, and a prolonged surgical time were associated with a significantly ($p < 0.005$) increased incidence of SSI. Group C showed the overall highest survival and lowest cumulative risk, but differences were not statistically significant. Conclusions: Group C showed the lowest incidence of infection in this sample. It is necessary to confirm these findings with larger studies.

Keywords: tibial; plateau; fracture; infection; prophylaxis; perioperative; cefuroxime; ceftriaxone; meropenem; teicoplanin



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1. Introduction

Surgical site infection (SSI) after tibial plateau definitive fixation is a serious complication that may negatively affect long-term outcomes related to this pathology [1,2]. The literature reports a higher SSI incidence related to tibial plateau fractures (2.5–12.3%) when compared to fractures in other locations (2.3% in pilon fractures or 3.6% in proximal femoral fractures) [3–6]. Different conditions have been related to a higher incidence of postoperative infection, for instance, prolonged surgical time, worse Schatzker classification fracture pattern, higher American Society of Anesthesiologists classification (ASA), open fractures, smoking, obesity, and the presence of diabetes mellitus. Based on this knowledge, the prevention of these infectious complications has met different approaches that have proven, in combination, to decrease the incidence of SSI, from reduction in surgical time to smoking cessation programs [7].

The administration of perioperative antibiotic prophylaxis is the cornerstone of the SSI prevention strategy regarding tibial plateau fracture surgery, in concordance with most prophylaxis guidelines [8]. The use of certain antimicrobial families, like cephalosporines and monobactams in the case of prophylaxis for open fractures, has been previously assessed in the literature [9], but to the best knowledge of the authors, there are no studies

that have assessed the effect of different perioperative antibiotic prophylaxes in surgical site infection incidence after tibial plateau fracture fixation.

The hypothesis of this study was that the use of different antibiotic prophylaxes may result in different effects regarding the incidence of postoperative SSI. The objective was to compare the impact of three different types of antibiotic prophylaxis on the postoperative incidence of SSI.

2. Materials and Methods

The aim of this study was to compare the impact of three different types of antibiotic prophylaxis on the postoperative incidence of SSI. This was a single-center retrospective cohort study performed at Hospital Clinic i Provincial de Barcelona, including all patients who underwent surgery for osteosynthesis of a tibial plateau fracture between January 2009 and November 2018. A minimum of two years of postoperative follow-up was required. We excluded those patients in which the presence of allergies prevented the administration of the standard antibiotic prophylaxis, since they required custom antibiotic protocols.

Three types of perioperative antibiotic prophylaxis during the study period were implemented in the following way: from 2009 to 2013 and following the stewardship guidelines, the standard prophylaxis used at our institution consisted of the administration of cephalosporins on monotherapy. From 2013 onwards, after a thorough revision of the literature was conducted by infectious diseases and epidemiology specialists of our center, the addition of teicoplanin established a two-drug prophylaxis strategy: cephalosporins plus teicoplanin, which was likewise alternated with an alternative two-drug strategy consisting of meropenem plus teicoplanin. This later combination was introduced after a surge in *Enterobacter cloacae*-related infections in one operation room and administered to patients who undergone surgery in said room onwards.

In accordance with the arguments explained beforehand, all patients included were divided into 3 groups. Group A received 1.5 g of cefuroxime iv before the skin incision as monotherapy. Patients from group B received a combination of 1g of meropenem iv + 0.8 g of teicoplanin iv at the beginning of the surgery, followed by 1g of meropenem iv after two hours into the surgery. Patients from group C received a combination of 1 g ceftriaxone iv + 0.8 g of teicoplanin iv at the beginning of the surgery, followed by an additional 1g of ceftriaxone iv after two hours into the surgery.

Additionally, patients presenting with open fractures received a three-day regimen of 1.5 g of cefuroxime/8 h + 240 mg of Gentamicin/24 h which was immediately administered at admission, independently of the perioperative prophylaxis given at the time of the definitive surgery.

Data were obtained through revision of standardized clinical records, including relevant information about patients' demographics (age and gender), injury mechanism, comorbidities, fracture pattern, presence of open fracture, need for external fixation as a bridge treatment before the definitive surgery, use of bone graft at the osteosynthesis, surgical time, type of intraoperative prophylaxis, occurrence of surgical site infection, time in weeks until the diagnosis of infection, and isolated microorganism on intraoperative culture. The presence of comorbidity was simplified using the ASA classification [10]. Fracture pattern was assessed using the Schatzker classification [11].

The surgical technique used was chosen by the orthopedic surgeon in accordance with the fracture pattern complexity. Patients were classified into having, or not, a prolonged surgical time regarding the 75th percentile of all the tibial plateau osteosynthesis procedures performed in our center during the period of the study, according to the National Nosocomial Infection Surveillance (NNIS) system risk index score [12].

The primary outcome was the incidence of SSI in each group. SSI was suspected in patients who presented fever, swelling, purulent discharge, wound dehiscence, augmented pain and elevation of serum leukocytes, erythrocyte sedimentation rate, or C-reactive protein after surgery. Failure was defined as the need for reintervention due to postoperative surgical site infection. Those patients with suspected SSI were treated with open debride-

ment and broad-spectrum intravenous antimicrobial regimen, which was maintained until definitive microbiological results were obtained. The definitive oral antibiotic treatment was selected according to the antibiogram results. Definitive diagnosis of SSI was defined by the presence of at least two positive cultures for the same microorganism isolated in samples obtained during the surgical debridement, or by the presence of a sinus tract.

Secondary outcomes were the most common microorganisms identified in cultures of patients with SSI.

Statistical Analysis

A confidence interval of 95% was previously established. The Kolmogorov–Smirnov test was used for assessing normal distribution. One-way ANOVA was performed for evaluation of homogeneity between groups. The chi-square test was performed to assess the independence of the different variables to the main outcome (presence of postoperative surgical site infection), since these variables could behave as confounding factors. Statistical significance was set at the 95% confidence level ($p < 0.05$). Risk and survival were assessed using Cox regression. All statistical tests were performed using the IBM Statistical Package for the Social Sciences v. 20.0 (SPSS® Inc., Chicago, IL, USA).

3. Results

Out of 163 patients initially revised, 10 cases were lost to follow-up and 5 cases received an alternative prophylaxis due to allergies, so a total of 148 cases were finally included in the study. Mean age (SD) was 47.9 (15.7) years old, with a male:female ratio of 1.4:1. Traffic accidents were reported as the most common injury mechanism (40.9%), followed by fall-from-standing low-energy injuries (19.4%). The main characteristics of the patients included in the study are shown in Table 1.

Table 1. General characteristics of the studied sample.

	n (%)
ASA Classification	
ASA 1	81 (55.0)
ASA 2	50 (33.5)
ASA 3	17 (11.4)
Schatzker Classification	
I	11 (7.4)
II	41 (27.7)
III	15 (10.1)
IV	12 (8.1)
V	33 (22.3)
VI	36 (24.3)
Open fracture	6 (4)
Mean (SD) surgical time (in minutes)	179.9 (72.4)
Patients with extended surgical time	37 (25)
Use of an internal fixation device	25 (16.9)
Use of bone graft	71 (47.9)

ASA: American Society of Anesthesiology. SD: standard deviation.

Up to 52 patients received intraoperative prophylaxis with cefuroxime (group A), 37 with the meropenem–teicoplanin combination (group B) and 59 with ceftriaxone–teicoplanin (group C). The general characteristics of each group are shown in Table 2.

Table 2. Characteristics of the three studied groups.

	Group A	Group B	Group C	<i>p</i> Value *
n	52	37	59	
Mean (SD) age	50.1 (15)	51.3 (15)	43.8 (15)	0.03
Male: female ratio	1.3:1	3:1	2.4:1	0.9
Mean ASA	1	2	1	0.001
Mean Schatzker	II	VI	II	0.6
Open fracture	1 (2%)	2 (5%)	3 (5%)	0.7
Use of external fixation	5 (9%)	5 (13%)	10 (16%)	0.8
Mean (SD) surgical time (in minutes)	157.5 (62)	185.3 (74)	188.5 (76)	0.2
Incidence of prolonged surgical time	7.6%	32.4%	28.8%	0.1
Use of bone graft	21 (40%)	20 (54%)	30 (50%)	0.3

ASA: American Society of Anesthesiology. * *p* value for One-way ANOVA. SD: standard deviation.

Out of the 148 included cases, a total of 20 patients (13.5%) presented SSI: 8 patients (15.4%) from group A, 8 patients (21.6%) from group B, and 4 patients (6.8%) from group C. Methicillin-sensible *Staphylococcus aureus* (MSSA) and *Enterobacter cloacae* were the most prevalent bacteria in group A, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* were most prevalent in group B, and *Pseudomonas aeruginosa* and *Staphylococcus epidermidis* were most prevalent in group C.

Group C was the group with the lowest postoperative infection rate and group B was the group with the longest time until infection ($p = 0.12$).

Factors significantly associated with a higher postoperative SSI were ASA III score ($p = 0.005$), Schatzker II classification ($p = 0.006$), use of external fixation as a bridge treatment (RR 2.9; $p = 0.008$), and a prolonged surgical time (RR 2.4; $p = 0.02$).

4. Discussion

There is a variation in the incidence of postoperative infection associated with tibial plateau fixation in the literature, ranging from 2.6 to 45.0% [6,12]. Systematic reviews like that of Henkelmann et al. [3] report an incidence of 12.3% after combining different sources. Postoperative infection in this sample is still higher than what is reported, and multiple factors could influence these findings, like higher ASA scores or many patients needing an external fixation bridge treatment (which means higher risk of soft tissue complications) [13–15]. In this context, the authors sought to highlight how Schatzker II-type fractures were associated with a higher risk of infection in this sample. The fact that the study was conducted at a training university hospital for residents, where less complex fracture patterns are usually treated by less experienced surgeons, entailed a longer surgical time related to this type of fractures, and thus a higher SSI rate. In fact, extended surgical time is consistently an independent variable associated with higher risk for infection, being constantly reported as such in the literature [6,13,16,17]. While it is known that extending the surgery by as little as half an hour can exponentially raise the infection risk [18], the baseline for every surgery's optimal duration is still blurred. Some orthopedic procedures like spine or distal tibia surgeries have well-established ideal surgical times [19,20] and others, like tibial plateau, still must use the NNIS system as a reference, which has proven to be poorly related to outcomes in this kind of surgery [6]. Because of the lack of this baseline, the evaluation of the surgical time in this sample is not optimal, which is a limitation of this study considering the importance of surgical time. In contrast to what is usually found in the literature [6,12,13], open fractures were not found to increase the risk of infection in this sample. The administration of wide spectrum antibiotics immediately following the arrival of infection in the emergency room may have a role in these findings. Additionally, patients with open fractures often waited for longer before definitive surgery with the intention of allowing soft tissue healing, so these patients could have undergone surgery with their soft tissues in better condition when compared to closed fracture patients, affecting the results.

Regarding perioperative prophylaxis, ceftriaxone–teicoplanin (group C) showed the lowest incidence of SSI even when adjusted by cofounding factors and compared against group A + group B patients. Ceftriaxone has high bactericidal speed, some resistance to betalactamases, elevated protein binding, and a long half-life [21]. Evidence suggests that ceftriaxone is a good alternative to safely cover methicillin-sensible *Staphylococcus aureus*, which was the most isolated microorganism in the tissue samples in this study, as well as in the literature [22,23]. Some evidence even suggests that ceftriaxone could become the treatment of choice for MSSA because it can be administered less frequently and has less toxicity [24].

The literature has reported an in vivo half-life of approximately 1 h for meropenem [25]. Considering that the group B prophylaxis was designed to be administered every 2 h, this could be why this group did not show a lower incidence of infection when compared to group C. Furthermore, some studies suggest that there could be an induction of meropenem-nonsensible *Pseudomonas aeruginosa* in certain patients if quinolones were previously used [26], and that it could also induce liver injury and beta-lactam cross-reactivity [27].

Studies found that despite cefuroxime target-attainment drug levels being reached after their perioperative administration, such levels could not be maintained in the immediate postoperative period, which could explain why it was insufficient as a monotherapy strategy [28]. In comparison, ceftriaxone levels seem to be higher but not enough to completely protect against *Pseudomonas* in monotherapy [29]. The combination of cefuroxime with glycopeptides could increase its effectiveness.

The present study features some inherent limitations. Most importantly, because of its retrospective nature, certain biases may have influenced the results. The retrospective design may have restricted the control over confounding variables and limited the amount of information that could be obtained. In addition, different treatments were not randomized. Even when most of the general characteristics of the groups were similar, there are still many variables that may have affected the results. Epidemiology of the microorganisms isolated in a hospital can vary with time, which in turn can make comparing prophylaxis administered in two different time frames, even if the study is single-centered, a limitation. Finally, the restricted number of cases because this was a single-center study addressing a low-prevalence pathology; thus, future studies are required to corroborate our findings. All these limitations may affect the extent to which our findings can be generalized beyond the specific cases studied. Nevertheless, the patient population from a large teaching hospital reflects a realistic representation of daily practice without exclusion of patients with relevant comorbidities.

It can be assumed that a large prospective randomized multi-center study approach should be performed to elucidate which prophylaxis strategy is more recommended.

5. Conclusions

Ceftriaxone–teicoplanin prophylaxis showed the lowest incidence of infection; however, these results were not statistically significant. Larger, prospective studies are needed to assess this subject.

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Abbreviations

SSI	surgical site infection
ASA	American Society of Anesthesiologists
NNIS	National Nosocomial Infection Surveillance
SPSS	Statistical Package for the Social Sciences
SD	Standard Deviation
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
MSSA	Methicillin-sensible <i>Staphylococcus aureus</i>
iv	Intravenous

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