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Withholding Preoperative Antibiotic Prophylaxis in Knee Prosthesis Revision: A Retrospective Analysis on Culture Results and Risk of Infection



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ABSTRACT

Background: A significant amount of patients undergoing revision surgery of a prosthetic joint turn out to have an infection. Withholding preoperative antibiotic prophylaxis in these patients to optimize culture yield during revision surgery remains a matter of debate. The aim of our study was to determine (1) the rate of positive intraoperative cultures with or without preoperative antibiotic prophylaxis and (2) the incidence of a prosthetic joint infection (PJI) during the follow-up in the 2 groups.

Methods: Medical files of patients in whom preoperative antibiotic prophylaxis was withheld until culture samples were taken (2007–2010, n = 284) and in whom antibiotic prophylaxis was given during the induction of anesthesia (2010–2013, n = 141) were retrospectively reviewed.

Results: The percentage of ≥ 1 positive cultures was the same in the group without (26%) and with preoperative prophylaxis (27%; *P* value, .7). PJI was diagnosed during revision surgery according to the Musculoskeletal Infection Society criteria in 6.7% patients not receiving preoperative prophylaxis and in 7.0% receiving it (*P* value, .79). We found no important differences in the type of microorganisms that were isolated in both groups. During a 3-month follow-up, an early PJI developed in patients undergoing total revision surgery in 6.4% of the nonpreoperative prophylaxis group vs 1.6% in the preoperative prophylaxis group (*P* value, .1).

Conclusion: Preoperative antibiotic prophylaxis does not reduce culture yield in patients undergoing knee revision surgery. Our data show a trend toward a higher PJI rate in the postoperative period of total revision surgery when preoperative prophylaxis is withheld.

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Diagnosing a prosthetic joint infection (PJI) remains a clinical challenge, especially in patients with a chronic, low-grade infection. In this patient category, evident clinical and biochemical signs

indicative for an infection may be absent [1–3]. In addition, preoperative synovial fluid cultures can be false negative and, therefore, may be difficult to interpret [4]. As a consequence, around 10% patients with loosening of the prosthesis, who preoperatively were considered to be aseptic, finally turn out to have an infection during revision surgery [5,6]. Therefore, obtaining reliable culture results during revision surgery is of utmost importance not only for diagnosis but also for starting an effective antibiotic treatment as soon as possible. To obtain reliable culture results, it is generally accepted that antibiotics should be withheld for at least 2 weeks before revision surgery [7,8]. However, withholding preoperative prophylaxis until tissue samples are obtained to optimize culture

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yield remains a matter of debate. In patients undergoing a revision surgery of a knee prosthesis, the incidence of PJI during follow-up is high, varying between 5% and 10% [9,10]. This is partly explained by suboptimal host factors but may also be the result of postponing antibiotic prophylaxis or—contrarily—because of the administration of antibiotic prophylaxis with subsequent false-negative cultures. As a result, deciding to give or not to give prophylaxis during the induction of anesthesia remains a diagnostic and ethical dilemma. For decades, antibiotic prophylaxis is considered as one of the most important cornerstones in the prevention of surgical site infections. Moreover, several studies have shown that when the timing of antibiotic prophylaxis is inadequate, the risk of developing a surgical site infection significantly increases [10–14].

In our center, from 2007 to 2010, prophylactic antibiotics were withheld until tissue samples were obtained. After 2010, it was decided to abandon this approach, as more sensitive culture methods became available and more data indicated the importance of preoperative prophylaxis [15]. By comparing these 2 cohorts of patients, we are able to address the aforementioned concerns about culture yield and the risk of infection. Hence, we retrospectively analyzed the medical files of patients who underwent a knee prosthesis revision, and determined (1) the diagnostic culture yield in patients with and without preoperative antibiotic prophylaxis (primary objective) and (2) the incidence of PJI during the follow-up of these patients in the postoperative period (secondary objective).

Materials and Methods

Inclusion Criteria

We retrospectively analyzed the medical files of patients between 2007 and 2013 who underwent a revision surgery of the knee. We included patients with a clinical suspicion of aseptic loosening and/or chronic pain at the site of the prosthesis that required total or partial revision of the prosthesis. Only patients who met the preoperative criteria for aseptic loosening were reviewed. The criteria for aseptic loosening were local pain, radiologic signs of loosening, and the absence of inflammatory symptoms. These symptoms included fever, local erythema, swelling, and/or fistulae. In all the patients presenting with loosening and/or chronic pain with a stable implant, C-reactive protein (CRP) and erythrocyte sedimentation rate were used as a screening tool for infection. When abnormal (ie, CRP ≥ 1.5 mg/dL or erythrocyte sedimentation rate >30 mm/h), a ^{99m}Tc methyl diphosphate 3-phase bone scan, ^{99m}Tc -hexamethylpropyleneamine oxime-labeled white blood cell scintigraphy, and a culture of synovial fluid obtained by sterile aspiration were performed to increase the probability of diagnosing an infection. Patients with a positive white blood cell scintigraphy or positive culture of synovial fluid were excluded. We additionally included patients who required only a minor revision with an exchange of the (mobile) components. This last group comprised patients who required an exchange of the polyethylene because of an instability problem, and patients who required resurfacing of the patella because of the anterior knee pain.

Antibiotic Prophylaxis

During the last several years, we used 3 different regimens of antibiotic prophylaxis in our center. (1) Between 2007 and 2009, antibiotic prophylaxis was given after tissue cultures were obtained during revision surgery and consisted of 800 mg teicoplanin, 2 g of ceftazidime, and a second dose of ceftazidime (1 g) 2 hours after the first dose (nonpreoperative short prophylaxis group), (2) between 2009 and 2010, patients received the same prophylaxis, but it was

decided to prolong the administration of antibiotics using vancomycin 1 g per 12 hours and ceftazidime 2 g per 8 hours intravenously until the fifth postoperative day (nonpreoperative long prophylaxis group), and (3) between 2010 and 2013, the same protocol was maintained, but antibiotic prophylaxis was started during the induction of anesthesia (before the sampling of tissue cultures in the preoperative long prophylaxis group). For the analysis on culture yield, groups not receiving preoperative prophylaxis were considered together. The reason to choose for teicoplanin during the first stage of prophylaxis is because it can be safely administered within a shorter period to achieve adequate serum levels as soon as possible, without causing a “red man syndrome.” According to the protocol, none of the patients used antibiotic treatment in the 2 weeks before surgery. Patients with a definitive diagnosis of PJI, according to the intraoperative culture results, received 6 weeks of antibiotic therapy guided by the antibiogram.

Surgical Procedure

Between 2007 and 2013, there were no variations in the preoperative washing protocol, skin preparation, hand hygiene solutions, surgical techniques, use of gentamicin-loaded cement for implant fixation, surgical team, or operating theaters. The revision arthroplasties were performed in a non-laminar airflow operating room. Revision surgery was performed under limb ischemia with the patient in the supine position. Previous incisions were used when possible. Dependent on the degree of loosening, a total or partial replacement of the prosthesis was performed, or only a change of (mobile) components was performed. In case of difficulty removing the prosthesis, an osteotomy of the anterior tibiae tuberosity was performed. Antibiotic-loaded cement was used for implant fixation as standard for revision knee arthroplasty. Total and partial revision arthroplasties were cemented with Cemex Genta from Tecres Medical (Verona, Italy), containing the equivalent of 1 g of gentamicin. No tissue grafts were necessary. Drains were removed within the 48 hours after the surgery.

Cultures and Outcome Parameters

During revision surgery, 5 tissue samples and 1 synovial fluid sample were obtained for culture. Synovial fluid was inoculated into aerobic and anaerobic blood culture bottles (BACTEC 9400; Becton Dickinson, Franklin Lakes, NJ) and incubated for 5 days. Tissue samples were obtained from the subfascial tissue (1), the joint capsule (2), the proximal interface (1), and the distal interface (1) of the prosthesis. Each culture was transported, processed, and analyzed using standard procedures. No changes were made in the diagnostic protocol during the study period. Unfortunately, sonication of the prosthesis was not yet performed in our hospital between 2007 and 2013. After being discharged, patients were followed at regular intervals at the outpatient clinic according to our protocol, which includes visits 2 weeks, 1 month, 3 months, 6 months, and 1 year after surgery. PJI was defined according to the current diagnostic criteria by the Musculoskeletal Infection Society [16]. An early PJI was defined as a PJI that occurred within the first 3 months after surgery [17].

Statistical Analysis

Comparison between groups was analyzed using an independent Student *t* test for continuous variables. The Levene test was used to test for equality between variances. For categorical variables, a chi-square test was used. A Fisher exact test was performed when appropriate. A *P* value $<.05$ was considered as statistically

significant. Statistical analysis was performed using SPSS, version 20.0 (SPSS Inc, Chicago, IL).

Results

Patient Characteristics

We included 425 patients in our analysis. Table 1 shows the patient characteristics of the preoperative prophylaxis (n = 141) and the nonpreoperative prophylaxis group (n = 284). Except for hypertension and cardiovascular disease, which occurred more in the preoperative prophylaxis group, no other differences were observed in patients' comorbidities. The degree of inflammation before revision surgery, depicted as the CRP, was similar between both groups. A trend toward a higher CRP was observed in the preoperative prophylaxis group (0.89 mg/dL; standard deviation, 2.15) vs the nonpreoperative prophylaxis group (0.61 mg/dL; standard deviation, 0.9; P value, .06). There was a large difference between the amounts of total revisions that were performed in both groups: 48% in the preoperative prophylaxis group vs 81% in the nonpreoperative prophylaxis group (P < .001). This could be explained by the fact that our hospital is a reference center, and every year, the number of total, partial, and minor revisions varies according to the needs of our reference area. In both patient groups, ≥5 intraoperative cultures were obtained in the majority of patients (≥93%).

Table 1
Patient Characteristics.

Characteristics	Nonpreoperative Prophylaxis (n = 284)	Preoperative Prophylaxis (n = 141)	P Value
Gender, n (%)			
Male	62 (22)	32 (23)	.84
Female	222 (78)	109 (77)	.84
Age, mean (SD), y	72 (8)	72 (9)	.41
BMI, ^a mean (SD), kg/m ²	31 (5)	31 (5)	.91
Comorbidity, n (%)			
Hypertension	179 (63)	104 (74)	.03 ^b
Diabetes mellitus	43 (15)	20 (14)	.72
Renal insufficiency	11 (4)	6 (4)	.99
Liver cirrhosis	6 (2)	6 (4)	.25
Cardiovascular disease	26 (9)	30 (21)	<.001 ^b
COPD	37 (13)	13 (9)	.14
Rheumatoid arthritis	6 (2)	1 (1)	.39
Medication, n (%)			
Corticosteroids	31 (5)	3 (2)	.17
Anticoagulants	17 (6)	8 (6)	.99
ASA classification, n (%)			
Class I-II	227 (80)	109 (77)	.48
Class III-IV	57 (20)	32 (23)	.48
Preoperative CRP, mean (SD), mg/dL, n (%)	0.6 (0.9)	0.9 (2.2)	.06
>1.0	43 (15)	25 (18)	.53
>1.5	31 (11)	20 (14)	.38
>2.0	20 (7)	14 (10)	.29
Revision surgery, n (%)			
Total revision	230 (81)	68 (48)	<.001 ^b
Partial revision	28 (10)	20 (14)	.19
Minor revision ^c	26 (9)	54 (38)	<.001 ^b
Total no. of cultures obtained, n	1595	825	
≥5 Cultures obtained per patient	261 (92)	133 (94)	.30
Days of hospitalization, mean (SD)	7.4 (3.8)	6.5 (3.4)	<.001 ^b

ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; SD, standard deviation.

^a Total patients for whom BMI was available: with prophylaxis n = 40 (28%), without prophylaxis n = 20 (7%).

^b P value <.05 was considered as statistically significant.

^c This group comprises patients who underwent an exchange of mobile components and/or resurfacing of the patella as described in the [Materials and Methods](#) section.

Table 2
Culture Yield.

	Nonpreoperative Prophylaxis (n = 284)	Preoperative Prophylaxis (n = 141)	P Value
Positive cultures, n (%)	73 (26)	38 (27)	.78
1 Culture positive	230 (81)	111 (79)	.92
2 Cultures positive	42 (15)	18 (13)	.86
3 Cultures positive	3 (1)	7 (5)	.22
4 Cultures positive	0 (0)	0 (0)	>.99
5 Cultures positive	0 (0)	0 (0)	>.99
6 Cultures positive	9 (3)	4 (3)	>.99
PJI diagnosed, ^a n (%)	19 (6.7)	10 (7.1)	.88
Total revision	13 (4.6)	7 (5.0)	.93
Partial revision	3 (1.1)	0 (0)	.18
Minor revision ^b	3 (1.1)	3 (2.1)	.37

MSSIS, Musculoskeletal Infection Society; PJI, prosthetic joint infection.

^a PJI was diagnosed according to the MSSIS criteria.

^b This group comprised patients who underwent an exchange of mobile components and/or resurfacing of the patella as described in the [Materials and Methods](#) section.

Primary Objective: Culture Yield

Table 2 shows the results on culture yield in the preoperative prophylaxis and the nonpreoperative prophylaxis group during revision surgery. From the culture positive patients (n = 111), 80% of these patients only had 1 positive intraoperative culture, and thus, the culture was considered as a contaminant. These cultures mainly consisted of *Staphylococcus epidermidis* (80%) and *Corynebacterium* species (7%). This finding was similar in both groups. According to the Musculoskeletal Infection Society criteria, a PJI was diagnosed in 7.1% of preoperative prophylaxis group vs 6.7% in the nonpreoperative prophylaxis group (P value, .79). Seventy percent of the PJIs that were diagnosed was observed in patients who received a total revision of the prosthesis. There was no difference in the amount of positive cultures during revision surgery between both groups (preoperative prophylaxis group: 27% vs 26% culture positivity in the nonpreoperative prophylaxis group; P value, .7). In addition, apart from more contaminants with *Bacillus cereus* that was observed in the prophylaxis group, the cultured microorganisms were the same between groups (Fig. 1).

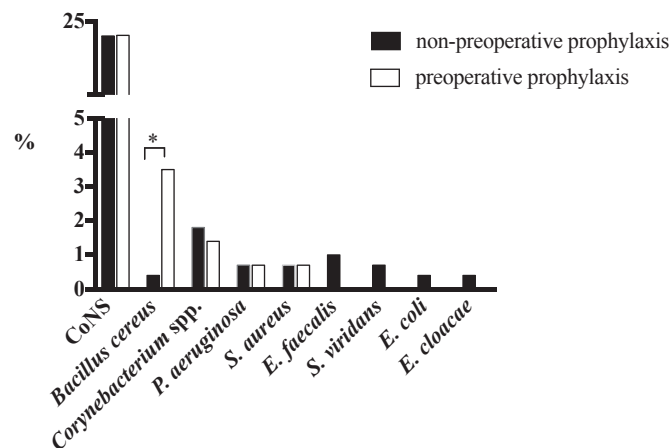


Fig. 1. Culture yield. The percentage of cultured microorganisms in the nonpreoperative prophylaxis group and the preoperative prophylaxis group. *P value <.05. CoNS, coagulase-negative staphylococci.

Secondary Objective: Risk of PJI After Surgery

Patients with a final diagnosis of PJI according to intraoperative cultures received 6 weeks of antibiotic treatment, and no one developed a PJI during follow-up. Therefore, this group was not included in this analysis, and the final number of patients evaluated was 396. None of the patients who underwent a partial or minor revision developed an early PJI during follow-up. In patients who underwent a total revision surgery ($n = 279$, 70%), an early PJI developed in 6.4% of the nonpreoperative prophylaxis group vs 1.6% in the preoperative prophylaxis group (P value, .1). Because we used 2 different antibiotic regimes in the nonpreoperative prophylaxis group as described in the Materials and Methods section, we additionally depicted the outcome of patients in these 3 different categories (Fig. 2). In the nonpreoperative short prophylaxis group, a PJI developed in 8% patients in the postoperative period. In the long nonpreoperative prophylaxis group, the rate of an early PJI was 4.7% (P value, .08). In the patients who received preoperative long prophylaxis, 1.6% of the patients developed an early PJI (P value, .08).

Discussion

A significant amount of patients undergoing a revision of a prosthetic joint, and who were considered as “aseptic” before surgery, turn out to have an infection [5,6]. Therefore, in these patients, a balanced decision should be made whether culture yield should be optimized by withholding preoperative prophylaxis or whether preventing a PJI should be prioritized by giving preoperative prophylaxis. In a large cohort of 425 patients, we retrospectively analyzed the difference in culture yield and outcome of patients in whom preoperative prophylaxis was given in comparison with patients in whom preoperative prophylaxis was withheld. We did not find any differences in culture yield between both groups. Although not statistically significant, we did observe a trend toward a higher rate of PJI in the early postoperative period in the nonprophylaxis group. Based on these findings, we recommend maintaining preoperative prophylaxis in patients undergoing an aseptic revision of a prosthetic joint.

One of the limitations of our study is the retrospective study design. In addition, we cannot rule out selection bias, as patients were consecutively enrolled over an extended period of time. However, no changes were made in the diagnostic or surgical approach, and the antibiotic regime and patient selection were

the same in the study period. Although our patients did not serve as their own control, our findings on culture yield are in agreement with studies with a different study design [18–22]. For example, several studies compared the preoperative culture results of synovial fluid with intraoperative findings [18,19,22]. Burnett et al [18] demonstrated in 26 knee revisions, a 100% culture yield despite preoperative prophylaxis. In all these patients, still more than 2 tissue cultures were positive during revision surgery and, therefore, did not hamper the ability to diagnose a PJI. This high diagnostic performance was also observed in a recent study by Pérez-Prieto et al [19], including hip, knee, and shoulder revisions. In addition, Tetreault et al [20] showed—in a randomized trial—that the sensitivity of intraoperative tissue cultures was 83%, using preoperative aspiration as a gold standard. This sensitivity was the same in patients in whom preoperative antibiotic treatment was withheld. Although all these patients had positive synovial fluid culture samples before surgery and thus suggesting a high bacterial load with a lower chance of false-negative culture results, our data suggest that culture yield is also not affected in patients with a lower a priori chance of an infection. In addition, Bedencić et al [21] performed an interesting study in which tissue samples were obtained after arthrotomy and again later during the procedure after the administration of antibiotic prophylaxis, using the same surgical area. The concentration of antibiotics was measured in the tissue to ensure adequate prophylaxis was given. The authors observed a similar diagnostic accuracy, as in the aforementioned studies, of 83%. In this study, false-negative cultures were found in patients with, in general, low-grade microorganisms (ie, *Propionibacterium acnes*, *Corynebacterium* species, and coagulase-negative staphylococci). However, sensitive diagnostic methods, like sonication, were not used in this study. We did not find any difference in culture yield for *Corynebacterium* species or coagulase-negative staphylococci in our cohort.

Even if certain low-grade microorganisms are missed during revision surgery, our data indicate the importance of preoperative prophylaxis. To the best of our knowledge, we are the first who show the infection rate of withholding preoperative prophylaxis in patients undergoing revision surgery of the knee. In our cohort, an early PJI was not observed in patients undergoing a partial or minor revision, probably owing to the less-invasive character of the surgery. However, in 6.4% patients who underwent a total revision, an early PJI developed in the nonpreoperative prophylaxis group. This rate was only 1.6% in the patients receiving preoperative antibiotic prophylaxis. Although these numbers were not statistically significant, the protective effect of preoperative prophylaxis is consistent with previous data in orthopedic surgery concerning the decrease in surgical site infections [10–12]. The development of a PJI in our study could be underestimated, since we did not study the development of late infections (>3 months postoperative). However, the majority of infections after arthroplasty occur within the first 3 months [23] supporting the change made by the National Healthcare Safety Network in January 2013 to use a 90-day surveillance period for these procedures.

In conclusion, withholding preoperative prophylaxis to maximize culture yield is probably not as critical as previously postulated. In addition, although no hard conclusion can be drawn due to the lack of statistical power, we did observe a trend toward a higher PJI rate in the early postoperative period in patients undergoing a total revision of a knee joint. Altogether, we would recommend the maintenance of preoperative prophylaxis in knee revision arthroplasties.

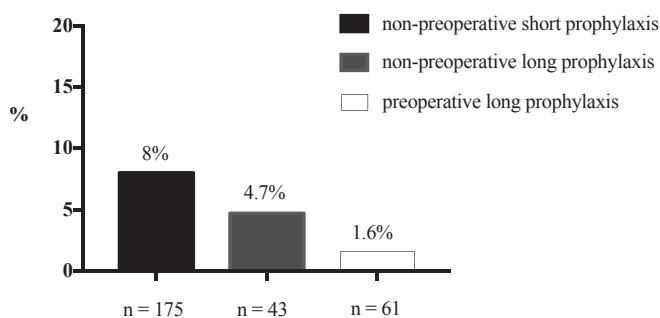


Fig. 2. Outcome on the development of an early prosthetic joint infection (PJI) in the nonpreoperative prophylaxis group and the preoperative prophylaxis group during follow-up in patients who underwent a total revision surgery ($n = 279$). Patients who were diagnosed with a PJI during revision surgery were not included in the analysis; none of these patients developed a PJI during follow-up.

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