Duration of Prophylactic Antibiotic and Prosthetic Joint Infection in a Developing Country: a Retrospective Cohort Study

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Abstract

Background

Perioperative antibiotic prophylaxis is one of the standard measures for preventing periprosthetic joint infection (PJI). In developing countries, poor surgical environment and patient hygiene are often cited as reasons for prolonged antibiotic duration without any evidence to support its effectiveness. The aim of this study was to investigate the infection rate after TKA compared between standard course (≤ 24 hours) and extended course (> 24 hours) of perioperative antibiotic prophylaxis in a developing country.

Methods

This retrospective study included patients who underwent unicompartmental knee arthroplasty or total knee arthroplasty during January 2013 to December 2018. A total of 3,316 patients were included. Of those, 1,284 and 2,032 patients received standard and extended course of antibiotic prophylaxis, respectively. The incidence of PJI was compared between groups, and we also analyzed for factors significantly associated with PJI.

Results

PJI developed in 0.5% (6/1,284) of the standard course group, and in 1.2% (24/2,032) of the extended course group. The difference and 95% confidence interval for the difference between groups was -0.714% (-1.338% to -0.043%), which confirms the noninferiority status of the standard course group compared to the extended course group. Longer hospital length of stay significantly associated with higher infection rate ($p=0.000$). Postoperative wound infection was not found to be associated with age, body mass index, American Society of Anesthesiologists classification, blood transfusion, or surgery type.

Conclusion

Twenty-four hours of perioperative antibiotic prophylaxis was found to be adequate for PJI prevention in a developing country setting.

Trial registration

Ethical approval and consent to participate: The study was approved by the Institutional review board of Siriraj Hospital, Mahidol university. [SIRB 847/2559(EC3)]

Introduction

Total knee arthroplasty (TKA) is the most frequently performed operative procedure among older adults. Periprosthetic joint infection (PJI) is one of the most feared complications after TKA with an estimated risk ranging from 0.39–2% worldwide. [1–3] Presenting features include pain, swelling, redness, and warmth of the knee joint. Treatment of PJI requires surgical revision and prolonged hospitalization, which

leads to considerable morbidity and mortality, particularly among those with advanced age. Multi-study analysis reported that sepsis (odds ratio [OR]: 8.73) and death (OR 3.25) were significantly higher in patients undergoing revision for PJI compared to those without infection. [3] Factors that were found to influence PJI included patient factors, such as diabetes mellitus (DM), obesity, anemia, American Society of Anesthesiologists (ASA) class ≥ 3 , malnutrition, and procedural factors, such as prolonged surgery and antibiotic prophylaxis. [2–6] Measures to promote PJI prevention after TKA include patient status improvement, such as blood sugar control in diabetic patients, nutritional therapy, and intraoperative and postoperative care. [6]

Perioperative antibiotic prophylaxis is accepted as the standard protocol for reducing the rate of superficial wound infection and PJI after TKA. The microorganisms that most commonly cause postoperative infection are Gram-positive bacteria, including *Staphylococcus aureus*, coagulase-negative staphylococcus (*S. epidermidis*), and group B streptococcus. Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important causative pathogen necessitating reoperation of primary TKA after debridement with polyethylene liner exchange due to infection. [7] The International Consensus on Periprosthetic Joint Infection [8] and the Society for Healthcare Epidemiology of America [9] recommends 24 hours of antibiotic prophylaxis for infection prevention after primary TKA. A systematic review and meta-analysis of randomized controlled trials that compared single-dose and multiple-dose antibiotic prophylaxis for surgical site infection (SSI) in major surgery found neither of those dosing regimens to be significantly associated with decreased risk of SSI. [10] In addition to the increased risk of antimicrobial resistance and drug toxicity, prolonged antibiotic treatment increases the financial burden on both self-paying patients and the healthcare system.

Even though the recommended duration of postoperative prophylactic antibiotics is 24 hours, the majority of cases in developing countries are prescribed a prolonged course for reasons that include poor hygiene, low socioeconomic status, low patient education level, and limited availability of healthcare workers and medical supplies. In Thailand, there are various protocols for prophylactic antibiotics depending on the surgeon's preference. The purpose of this study was to perform a retrospective review in a public hospital that provides care to patients from all socio-economic backgrounds. Two groups of patients receiving standard (≤ 24 hours) and extended course (> 24 hours) of antibiotics following TKA were compared. The specific aim of this study was to determine whether prolonged duration of antibiotics can reduce the infection rate after TKA compared with the standard 24-hour course of perioperative antibiotic prophylaxis.

Methods

Ethics and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations.

Patients and study design

This retrospective study was conducted at a tertiary university hospital, single center. After receiving Institutional Review Board approval (COA no. 847/2559(EC3)), the medical records of patients diagnosed with osteoarthritis of the knee who underwent unicompartmental knee arthroplasty (UKA) or total knee arthroplasty (TKA) during January 2013 to December 2018 were reviewed. Unilateral and bilateral surgery patients were both eligible for inclusion. The inclusion criterion was the knee arthroplasty performed for primary osteoarthritis or secondary osteoarthritis. Patients were excluded if they received revision knee arthroplasty, were administered systemic antibiotics more than 60 minutes before or after skin incision, had a follow-up time less than 3 months, or had incomplete medical information.

The national recommendation for prevention of SSI was applied. Patients with a body weight < 80 kg received a single-dose of cefazolin 1 gram intravenously within 60 minutes before skin incision, and three additional doses during the first 24 hours after operation. A single-dose of cefazolin 2 grams was considered optimal for patients weighing > 80 kg. Vancomycin or clindamycin was alternatively prescribed if patients had a history of cephalosporin allergy. Other antimicrobial prophylaxis was given according to surgeon's preference and intraoperative findings. The surgical limb was painted with either povidone-iodine or chlorhexidine with alcohol, and the surgical site was covered with a *3M Loban 2 Antimicrobial Incise Drape* (3M Company, St. Paul, MN, USA). A pneumatic tourniquet was inflated during the procedure and deflated after wound closure or when the duration of tourniquet exceeded 120 minutes. All surgeons routinely used double gloves.

Demographic and clinical patient characteristics, such as gender, age, body mass index (BMI), comorbidities, and American Society of Anesthesiologists (ASA) score, were recorded. Operative data, such as surgery type, type of antibiotic prophylaxis, duration of antibiotic prophylaxis, blood transfusion and length of hospital stay were reviewed from medical records during the primary surgical period. Patients were divided according to the amount of time they received antibiotic prophylaxis. The standard course group included patients who received antibiotic for less than or equal to 24 hours after surgery, and the extended course group consisted of patients who received antibiotic for longer than 24 hours after surgery.

The primary outcome in this study was the incidence of PJI after knee arthroplasty according to the diagnosis criteria by the Musculoskeletal Infection Society (MSIS) 2011 [11] and modified to international consensus review (International Consensus on Musculoskeletal Infection (ICM)) in 2013 [12]. The diagnosis of PJI was made by the attending physician during admission period for treatment of PJI.

Sample size calculation and statistical analysis

For non-inferiority test calculation and assuming an infection rate between groups of 1% ($\delta = 0.01$), an inferiority margin of 0.01, and type-1 (α) and type-2 errors (β) of 0.05 and 0.2, respectively, at the ratio 1:1 of population between group 1 ($\leq$ 24-hours of postoperative prophylactic antibiotics) and group 2 ($>$ 24-hours postoperative prophylactic antibiotics), the calculated sample size required $n = 1,225$ patients per group. In our study the total sample size was 3,316 (1,284 in group 1, and 2,032 in group 2.)

Student's t-test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare dichotomous variables. Continuous data are presented as mean plus/minus standard deviation, and categorical data are given as number and percentage. A p-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS Statistics version 18 (SPSS, Inc., Chicago, IL, USA).

Results

Of the 3,374 patients with osteoarthritis of the knee who underwent UKA or TKA at our center during the study period, 58 patients were excluded. Of those, revision arthroplasty was performed in 15 cases, 3 cases were lost to follow-up, and 40 cases had incomplete medical information. The remaining 3,316 patients were included, and those patients were categorized into the standard course group (≤ 24 hours) or the extended course group (> 24 hours). There were 1,284 (38.7%) patients in the standard course group, and 2,032 (61.2%) patients in the extended course group. (Figure.1) The mean age at the time of operation was 69.5 ± 8.5 years and 68.6 ± 8.4 years in the standard course and the extended course groups, respectively. Even though the difference in age between the standard and extended groups was statistically significant (69.5 ± 8.5 vs. 68.6 ± 8.4 , respectively; $p = 0.006$), there was no statistical significance between groups when we stratified age as < 69 and ≥ 70 years. Concerning the choice of antibiotic, fosfomycin and cefuroxime (Zinacef) were prescribed significantly more often among patients who were prescribed antibiotic prophylaxis for 48 hours. Demographic and clinical characteristics of patients compared between the standard course and extended course groups are shown in Table 1.

Table 1
Demographic and clinical characteristics of patients compared between the standard course and extended antibiotic course groups (N = 3,316)

Characteristics	ATB ≤ 24 hours (n = 1,284)	ATB > 24 hours (n = 2,032)	p-value
Age (years)	69.5 ± 8.5	68.6 ± 8.4	0.006
Age (years)			
- ≤ 69	703 (54.8%)	1,164 (57.3%)	
- > 70	581 (45.2%)	868 (42.7%)	0.159
Antibiotic			
- Cefazolin	1,178 (91.7%)	782 (38.5%)	
- Clindamycin	52 (4.1%)	60 (3.0%)	< 0.001
- Fosfomycin	20 (1.6%)	972 (47.8%)	
- Zinnacef	31 (2.4%)	212 (10.4%)	
- Miscel	3 (0.2%)	6 (0.3%)	
Blood transfusion			
- Yes	1,102 (85.8%)	1,777 (87.5%)	
- No	182 (14.2%)	255 (12.5%)	0.178
Hospital length of stay (days)	5.9 ± 2.5	5.3 ± 1.8	< 0.001
Body mass index (kg/m ²)	27.1 ± 4.4	27.3 ± 4.2	0.275
ASA classification			
- 1	84 (6.5%%)	121 (6.0%)	
- 2	884 (68.9%)	1,476 (72.6%)	0.035
- 3	316 (24.6%)	431 (21.2%)	
- 4	0 (0.0%)	4 (0.2%)	

Data presented mean ± standard deviation or number and percentage

A p-value < 0.05 indicates statistical significance

Abbreviations: ASA, American Society of Anesthesiologists; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty

Characteristics	ATB ≤ 24 hours (n = 1,284)	ATB > 24 hours (n = 2,032)	p-value
Follow-up (months)			
- 0–3	12 (0.9%)	9 (0.4%)	0.555
- 3–6	105 (8.2%)	175 (8.6%)	
- 6–12	871 (67.8%)	1,367 (67.3%)	
- 12–24	221 (17.2%)	359 (17.7%)	
- 24–36	75 (5.9%)	122 (6.0%)	
Procedure			
- TKA	1,203 (93.7%)	1,736 (85.4%)	< 0.001
- UKA	81 (6.3%)	296 (14.6%)	
Data presented mean ± standard deviation or number and percentage			
A p-value < 0.05 indicates statistical significance			
Abbreviations: ASA, American Society of Anesthesiologists; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty			

The primary outcome was the difference in the rate of infection between patients who received $\leq$ 24 and > 24 hours of antibiotic prophylaxis. PJI developed in 0.5% (6/1,284) of the standard course group, and in 1.2% (24/2,032) of the extended course group. The difference and 95% confidence interval for the difference between groups was - 0.714% (-1.338% to -0.043%), which confirms the noninferiority status of the standard course group compared to the extended course group. Analysis for factors significantly associated with PJI is shown in Table 2. Longer hospital LOS was found to be significantly associated with PJI ($p = 0.000$). Postoperative wound infection was not found to be associated with age, BMI, ASA classification, blood transfusion, or surgical type.

Table 2
Analysis for factors significantly associated with surgical site infection

Factors	No infection (n = 3,286)	Infection (n = 30)	<i>p</i> -value
Hospital length of stay (days)	5.7 ± 2.2	8.2 ± 6.9	0.000
Age (years)	69.0 ± 8.4	68.0 ± 9.3	0.546
Body mass index (kg/m ²)	27.2 ± 4.3	28.1 ± 5.0	0.242
ASA classification			
- 1	203 (6.2%)	2 (6.7%)	0.728
- 2	2,338 (71.1%)	22 (73.3%)	
- 3	741 (22.6%)	6 (20.0%)	
- 4	4 (0.1%)	0 (0.0%)	
Blood transfusion			
- No	2,856 (86.9%)	23 (76.7%)	0.104
- Yes	430 (13.1%)	7 (23.3%)	
Procedure			
- TKA	2,911 (88.6%)	28 (93.3%)	0.486
- UKA	375 (11.4%)	2 (6.7%)	
Data presented mean ± standard deviation or number and percentage			
A <i>p</i> -value < 0.05 indicates statistical significance			
Abbreviations: ASA, American Society of Anesthesiologists; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty			

Discussion

TKA is a widely performed procedure with a high rate of success and a low complication rate. Though shortened hospital stays and improved surgical outcomes have been observed during the last decade, PJI remains a paramount concern. [13] Feng B, et al. reported the highest percentage of revision operations to be among patients that had SSI diagnosed during follow-up visits. [14] In addition to increased rates of morbidity and mortality, revision knee replacement is expensive. Antimicrobial prophylaxis has been proven to reduce the SSI rate in many types of surgery. The adverse effects of antibiotic overuse in arthroplasty surgery included worsened MRSA outbreak, increased incidence of *Clostridioides difficile* infection, and acute kidney injury. [15] A 24-hour course of antibiotic prophylaxis is considered enough to

prevent SSI by reducing transient bloodstream infection. [16, 17] Thus, the International Consensus on Periprosthetic Joint Infection recommended a 24-hour course for the prevention of surgical site infection.

Published studies and guidelines have suggested/recommended that the duration of antibiotic prophylaxis not exceed 24 hours. [8, 9] However, in clinical practice, the decision how to prescribe antibiotic prophylaxis in TKA or UKA surgery depend on many factors, such as surgeon's preference, drain usage, ambient temperature, degree of leukocytosis, hospital protocols, intraoperative findings, and patient perception. A study conducted in Canada showed that only 42% of orthopedic patients had antibiotics discontinued within 24 hours after surgery, and more than 70% of patients received > 72 hours of antibiotic after surgery in Taiwan. [18] In developing countries, many surgeons prefer to extend the course of antibiotic beyond 24 hours because their surgical environment, including operating rooms and surgical draping, failed to comply with the principles of surgical asepsis. Concerning patient-related factors, poor hygiene and history of high incidence of PJI also contributed to the decision regarding how to prescribe perioperative antibiotic prophylaxis. [19] To our knowledge, no study has investigated the incidence of PJI related to duration of ATB in developing countries. Our study compared the surgical outcomes of UKA and TKA patients between those who received antibiotic prophylaxis for ≤ 24 hours and those who received antibiotic prophylaxis for > 24 hours. Our results revealed no significant difference between groups for either superficial or deep SSI. Age at operation, BMI, ASA score, type of surgery, type of antibiotic drug, and hospital LOS were all found not to be significantly associated with infection following TKA. Blood transfusion appeared to increase SSI, but without statistical significance. Based on these findings, we recommend that antibiotic administration not exceed 24 hours to minimize adverse events associated with antimicrobial drugs, to save cost, and to reduce the length of hospital stay.

Nelson CL, et al. reported no statistically significant difference among patients with total joint arthroplasty (TJA) or hip fracture repair compared between those who received antibiotic for 24 hours or less, and patients who received antibiotic for more than 24 hours after surgery. [20] A double-blind multicenter study included 1,354 patients who underwent primary or revision TJA. One day of cefuroxime administration was compared with three days of cefazolin prophylaxis for surgical site infection. The infection rate was lower in patients who received antibiotics for 24 hours postoperatively in both TKA (0.6% vs. 1.4%) and total hip arthroplasty (THA) (0.5% vs. 1.2%). [21] A recent study in PJI following aseptic TKA revision demonstrated that first-generation cephalosporin prophylaxis for 24 hours did not result in a significantly different rate of infection compared with an extended course ($p = 0.14$). [22] Moreover, other studies demonstrated that postoperative antibiotic drug continuation with multiple dosing regimen is not more effective than single-dose regimen for preventing SSI or PJI. [23–25] In contrast, recent evidence suggested that prolonged oral antibiotic prophylaxis for up to 1 week may yield benefit in high-risk patients, especially in those with comorbidities that are associated with increased susceptibility to infection, by reducing the incidence of infection within 90 days following TJA. [26]

Blood transfusion was not found to be a significant risk factor for PJI in our study. We found infection rates of 2.2% and 0.8% in patients with and without blood transfusion, respectively. In contrast, a recently

published study that investigated for risk factors significantly associated with PJI after TKA found red blood cell (RBC) transfusion to be a significant risk factor for postoperative infection (OR: 4.60). Other significant risk factors for PJI and TKA found in that study included prolonged operative time (> 90 minutes), tourniquet time (> 60 minutes), non-antibiotic-laden cement use, obesity (BMI > 30 kg/m²), diabetes, and ASA grade $\geq$ 3. [27]. In another study, surgical site infection developed in 2.82% of patients who received red blood cell (RBC) transfusion, but in only 0.4% of those who did not. [28]

This study has some limitations that should be disclosed. The first limitation is our study's retrospective design, many confounding factors cannot be controlled. The second is that our groups were not equal in size. The extended course group was approximately 2 times larger than the standard course group. Third, the baseline characteristics of our patients were different from those reported in other studies, so comparisons between our study and other studies should take this factor into account. Fourth and last, we did not perform multivariate analysis to exclude potentially confounding factors. Having acknowledged those limitations, our finding that standard course is not inferior to extended course of antibiotic prophylaxis against postoperative PJI is consistent with the findings of previously reported studies.

Conclusion

No significant difference in the incidence of PJI was observed between the standard course and extended course of perioperative antibiotic prophylaxis groups. Longer hospital LOS was the only factor found to be significantly associated with PJI. Despite the study setting being in a developing country with lower hygiene standards, our results are consistent with prior evidence that an extended course of antibiotic prophylaxis does not reduce PJI. According to these results, surgeons should not resort to prolonging the course of antibiotic prophylaxis as a complement to aseptic technique. A 24-hour course of perioperative antibiotic prophylaxis was shown to be adequate for preventing PJI without increasing the emergence of drug-resistant pathogens, the cost, or the hospital LOS.

Declarations

- Ethical approval and consent to participate: The study was approved by the Institutional review board of Siriraj Hospital, Mahidol university. [SIRB 847/2559(EC3)]
- Informed consent was obtained from all individual participants included in the study.
- Ethics and consent to participate: All methods were carried out in accordance with relevant guidelines and regulations.
- Consent for publication: All authors have read and approved the final submitted manuscript.
- Availability of data and material: Requests for data not shown in the body of this manuscript can be made to the corresponding author
- Competing interests: The authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

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- Authors' contributions: Keerati Chareancholvanich M.D. provided research questions and write manuscript., Pakpoom Ruangsomboon, Waiwit Sanguanwongwan, Piyanuch Musikachart conducted data collection, analyzed data and discussion and developed the full manuscript. Chaturong Pornrattanamaneewong D., M.Sc. examined all data analysis, detailed the results, statistical calculation, monitored data and discussion. Rapeepat Narkbunnam M.D. also provided useful advice and finalize the manuscript.
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References

1. Chun KC, Kim KM, Chun CH. Infection following total knee arthroplasty. *Knee Surg Relat Res.* 2013;25(3):93-99. doi:10.5792/ksrr.2013.25.3.93
2. Teo BJX, Yeo W, Chong HC, Tan AHC. Surgical site infection after primary total knee arthroplasty is associated with a longer duration of surgery [published correction appears in *J Orthop Surg (Hong Kong)*. 2019 Jan-Apr;27(1):2309499019831607]. *J Orthop Surg (Hong Kong)*. 2018;26(2):2309499018785647. doi:10.1177/2309499018785647
3. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. *Clin Orthop Relat Res.* 2001;(392):15-23.
4. Bozic KJ, Lau E, Kurtz S, Ong K, Berry DJ. Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. *Clin Orthop Relat Res.* 2012;470(1):130-137. doi:10.1007/s11999-011-2043-3
5. Naranje S, Lendway L, Mehle S, Gioe TJ. Does operative time affect infection rate in primary total knee arthroplasty?. *Clin Orthop Relat Res.* 2015;473(1):64-69. doi:10.1007/s11999-014-3628-4
6. Ratto N, Arrigoni C, Rosso F, et al. Total knee arthroplasty and infection: how surgeons can reduce the risks. *EFORT Open Rev.* 2017;1(9):339-344. Published 2017 Mar 13. doi:10.1302/2058-5241.1.000032
7. Bene N, Li X, Nandi S. Factors affecting failure of irrigation and debridement with liner exchange in total knee arthroplasty infection. *Knee.* 2018;25(5):932-938. doi:10.1016/j.knee.2018.07.003
8. Parvizi J, Gehrke T, Chen AF. Proceedings of the International Consensus on Periprosthetic Joint Infection. *Bone Joint J.* 2013;95-B(11):1450-1452. doi:10.1302/0301-620X.95B11.33135
9. Anderson DJ, Podgorny K, Berríos-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol.* 2014;35(6):605-627. doi:10.1086/676022
10. McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust N Z J Surg.* 1998;68(6):388-396. doi:10.1111/j.1445-

11. Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res*. 2011;469(11):2992-2994. doi:10.1007/s11999-011-2102-9
12. Parvizi J, Gehrke T; International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. *J Arthroplasty*. 2014;29(7):1331. doi:10.1016/j.arth.2014.03.009
13. Sarpong NO, Boddapati V, Herndon CL, Shah RP, Cooper HJ, Geller JA. Trends in Length of Stay and 30-Day Complications After Total Knee Arthroplasty: An Analysis From 2006 to 2016. *J Arthroplasty*. 2019;34(8):1575-1580. doi:10.1016/j.arth.2019.04.027
14. Feng B, Weng X, Lin J, et al. *Zhonghua Wai Ke Za Zhi*. 2015;53(2):106-109.
15. Tande AJ, Patel R. Prosthetic joint infection. *Clin Microbiol Rev*. 2014;27(2):302-345. doi:10.1128/CMR.00111-13
16. Bosco JA, Bookman J, Slover J, Edusei E, Levine B. Principles of Antibiotic Prophylaxis in Total Joint Arthroplasty: Current Concepts. *J Am Acad Orthop Surg*. 2015;23(8):e27-e35. doi:10.5435/JAAOS-D-15-00017
17. Voigt J, Mosier M, Darouiche R. Systematic review and meta-analysis of randomized controlled trials of antibiotics and antiseptics for preventing infection in people receiving primary total hip and knee prostheses. *Antimicrob Agents Chemother*. 2015;59(11):6696-6707. doi:10.1128/AAC.01331-15
18. McDonald LC, Yu HT, Yin HC, Hsiung AC, Ho M; Antibiotic Use Working Group. Use and abuse of surgical antibiotic prophylaxis in hospitals in Taiwan. *J Formos Med Assoc*. 2001;100(1):5-13.
19. Moylan JA, Kennedy BV. L'importanza di camici e teli come barriera per prevenire le infezioni post-operatorie [Importance of surgical gowns and drapes as barriers for prevention of postoperative infections]. *Minerva Chir*. 1981;36(20):1365-1372.
20. Nelson CL, Green TG, Porter RA, Warren RD. One day versus seven days of preventive antibiotic therapy in orthopedic surgery. *Clin Orthop Relat Res*. 1983;(176):258-263
21. Mauerhan DR, Nelson CL, Smith DL, et al. Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am*. 1994;76(1):39-45. doi:10.2106/00004623-199401000-00006
22. Kuo FC, Lin PC, Bell KL, Ko JY, Wang CJ, Wang JW. Extended Postoperative Prophylactic Antibiotics with First-Generation Cephalosporin Do Not Reduce the Risk of Periprosthetic Joint Infection following Aseptic Revision Total Knee Arthroplasty. *J Knee Surg*. 2020;33(6):597-602. doi:10.1055/s-0039-1683889
23. Tang WM, Chiu KY, Ng TP, Yau WP, Ching PT, Seto WH. Efficacy of a single dose of cefazolin as a prophylactic antibiotic in primary arthroplasty. *J Arthroplasty*. 2003;18(6):714-718. doi:10.1016/s0883-5403(03)00201-8
24. Ryan SP, Kildow BJ, Tan TL, et al. Is There a Difference in Infection Risk Between Single and Multiple Doses of Prophylactic Antibiotics? A Meta-analysis. *Clin Orthop Relat Res*. 2019;477(7):1577-1590. doi:10.1097/CORR.0000000000000619

25. Tan TL, Shohat N, Rondon AJ, et al. Perioperative Antibiotic Prophylaxis in Total Joint Arthroplasty: A Single Dose Is as Effective as Multiple Doses. *J Bone Joint Surg Am.* 2019;101(5):429-437. doi:10.2106/JBJS.18.00336
26. Inabathula A, Dilley JE, Ziemba-Davis M, et al. Extended Oral Antibiotic Prophylaxis in High-Risk Patients Substantially Reduces Primary Total Hip and Knee Arthroplasty 90-Day Infection Rate. *J Bone Joint Surg Am.* 2018;100(24):2103-2109. doi:10.2106/JBJS.17.01485
27. Blanco JF, Díaz A, Melchor FR, da Casa C, Pescador D. Risk factors for periprosthetic joint infection after total knee arthroplasty. *Arch Orthop Trauma Surg.* 2020;140(2):239-245. doi:10.1007/s00402-019-03304-6
28. Klasan A, Dworschak P, Heyse TJ, et al. Transfusions increase complications and infections after hip and knee arthroplasty: An analysis of 2760 cases. *Technol Health Care.* 2018;26(5):825-832. doi:10.3233/THC-181324

Figures

Figure 1

Patient flow chart