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The AAHKS Clinical Research Award: Extended Oral Antibiotics Prevent Periprosthetic Joint Infection in High-Risk Cases: 3855 Patients With 1-Year Follow-Up

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Abstract

Background: Surgical and host factors predispose patients to periprosthetic joint infection (PJI) after primary total hip arthroplasty (THA) and total knee arthroplasty (TKA). While surgical factors are modifiable, host factors can be challenging, and there are limited data demonstrating that preoperative patient optimization decreases risk of PJI. The goal of this study was to evaluate whether extended oral antibiotic prophylaxis reduces the one-year infection rate in high-risk patients.

Methods: A total of 3855 consecutive primary THAs and TKAs performed between 2011 and 2019 at a suburban academic hospital with modern perioperative and infection-prevention protocols were retrospectively reviewed. Beginning in January 2015, a 7-day oral antibiotic prophylaxis protocol was implemented after discharge for patients at high risk for PJI. The percentage of high-risk patients diagnosed with PJI within 1 year was compared between groups that did and did not receive extended antibiotic prophylaxis. Univariate and logistic regression analyses were performed, with $P \leq .05$ denoting statistical significance.

Results: Overall 1-year infection rates were 2.26% and 0.85% after THA and TKA, respectively. High-risk patients with extended antibiotic prophylaxis had a significantly lower rate of PJI than high-risk patients without extended antibiotic prophylaxis (0.89% vs 2.64%, respectively; $P < .001$). There was no difference in the infection rate between high-risk patients who received antibiotics and low-risk patients (0.89% vs 1.29%, respectively; $P = .348$) with numbers available.

Conclusion: Extended postoperative oral antibiotic prophylaxis for 7 days led to a statistically significant and clinically meaningful reduction in 1-year infection rates of patients at high risk for infection. In fact, the PJI rate in high-risk patients who received antibiotics was less than the rate seen in low-risk patients. Thus, extended oral antibiotic prophylaxis may be a simple measure to effectively counteract poor host factors. Moreover, the findings of this study may mitigate the

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incentive to select healthier patients in outcome-based reimbursement models. Further study with a multicenter randomized control trial is needed to further validate this protocol.

Level of Evidence: Therapeutic level III.

Keywords

periprosthetic joint infection; extended antibiotics; primary total joint arthroplasty; primary total knee arthroplasty; primary total hip arthroplasty

Periprosthetic joint infection (PJI) is one of the most dreaded complications after primary total hip arthroplasty (THA) and total knee arthroplasty (TKA). It has an enormous impact on the health of patients, often leading to poor function and quality of life. Given the increased patient morbidity and mortality [1–5] associated with infection as well as the drastic economic implications [6–12] of revision surgery on patients, surgeons, and hospital systems, mitigating the risk of PJI is of crucial importance.

The current literature is replete with research from the past decade on surgical and host factors associated with PJI, particularly modifiable risk factors for prevention of infection [13–16]. Accordingly, most surgeons and institutions have adopted key prevention protocols to minimize postoperative infection. Of the modifiable risk factors identified for infection, controlling environmental factors is more readily achieved by the surgeon and health institution than the control of host factors. This is often due to the inherent nature of a patient presenting for total joint arthroplasty (TJA), often obese and sedentary because of pain and presenting with chronic medical conditions such as diabetes and kidney disease. Furthermore, there are few data to support that optimization of such host risk factors leads to decreased PJI rates [17–24].

While the PJI rate remains at 1%–2% after primary TJA [25–29], high-risk patients (patients with known risk factors) have been shown to have increased susceptibility to infection. These high-risk patients may benefit from additional preventative efforts to minimize the risk for PJI. Moreover, because of outcome-based reimbursement models, some surgeons and institutions are potentially incentivized to select for healthier patients [30–33], subsequently decreasing access to TJA for higher-risk patients.

Recent studies have supported the use of extended oral antibiotic prophylaxis after two-stage reimplantation to reduce recurrent PJI [34–38]. Our group explored the use of extended oral antibiotics for 7 days after primary TJA and demonstrated a reduction in 90-day infection rates in high-risk patients [39]. We hypothesized that this identical extended oral antibiotic prophylaxis protocol would reduce PJI rates in high-risk patients at one-year postoperatively.

Materials and Methods

Sample

Prospectively recorded data on 4278 consecutive primary TJAs performed between December 1, 2011 and March 31, 2019 by 4 fellowship-trained surgeons at the same suburban academic hospital using the same perioperative protocols were reviewed. The

hospital is a tertiary referral center for sicker patients who are at high risk for complications, including infection, after TJA.

The study was conducted with institutional board review approval. All patients who underwent primary THA or TKA for osteoarthritis were included. Four hundred and twenty-three patients were excluded because of potential confounders, including performance of the TJA as outpatient same-day surgery (n = 241); increased complexity of procedure (n = 94); non-PJI–related mortality within 1 year of surgery (n = 14); concurrent malignancy (n = 10); infection before surgery (n = 6); performed for acute fracture (n = 53), post-traumatic arthritis (n = 2), femoral neck malunion or nonunion (n = 1); intraoperative fracture (n = 1); and postoperative medical complication requiring readmission (n = 1).

Standard Perioperative Infection-Control Practices

Our institution's standardized preoperative prevention measures include nasal screening and decolonization, preoperative skin cleansing, glycemic control, a minimum of 3 months between steroid injection and surgery, and intravenous (IV) administration of antibiotics within an hour before surgery. Intraoperative preventative measures include the use of laminar airflow, alcohol and chlorhexidine-based cleansing of the surgical site, skin sealant and drapes, and dilute betadine (povidone-iodine) or dilute chlorhexidine soaks before closure. Normothermia is maintained, and supplemental oxygen is administered throughout the procedure. Antibiotic-impregnated bone cement is used in all cemented TKAs. IV antibiotics are administered for 24 hours after surgery. Allogeneic blood transfusions are not used.

Extended Antibiotic Prophylaxis for High-Risk Patients

All patients undergo medical clearance by a perioperative internal medicine specialist whose practice focuses exclusively on TJA. A comprehensive standardized history is recorded, and a thorough physical examination is performed along with detailed screening laboratory analysis, such as measurement of hemoglobin (Hgb) A1c and prealbumin levels. This information is reviewed in a weekly coordinated care conference to proactively develop patient care plans. Patients at high risk for postoperative PJI are identified at this time.

Beginning on January 1, 2015, we formalized a protocol by which patients at high risk for PJI on the basis of specific risk factors were given prophylactic oral antibiotics for 7 days after discharge. On July 13, 2016, the protocol was amended to add nasal colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and/or methicillin-sensitive *S aureus* as risk factors because decolonization protocols do not reliably eradicate colonization. Comorbidities identified as placing patients at high risk for infection are listed in Table 1. From January 1, 2015, onward, no additional changes were made to existing infection prevention protocols or perioperative protocols in general, thus isolating the effect of extended oral antibiotic prophylaxis on 1-year PJI rates.

One hundred and forty patients in our sample did not have any of the protocol risk factors outlined in Table 1 but received extended antibiotic prophylaxis because they were at risk for PJI as a result of other diseases or disorders clinically shown to weaken the immune system. These included a history of sepsis, hepatitis C, chronic recurrent cystitis, stasis dermatitis,

traumatic catherization with hematuria, and patients who underwent surgery within 3 months after cortisone intra-articular injection against recommendation. These risk factors are listed as “other” in Table 1.

The perioperative antibiotic of choice was IV cefazolin for 24 hours, including patients with a reported penicillin allergy. If a patient had a reported true anaphylactic allergy to cephalosporins specifically, they received IV clindamycin. If the patient tested positive for MRSA colonization, they were given dual antibiotics in the form of vancomycin and cefazolin. The extended oral antibiotic protocol for high-risk patients commenced on the day of discharge after inpatient IV antibiotics was completed. The oral antibiotic protocol consisted of cefadroxil, 500 mg twice daily for 7 days. Patients who tested positive for MRSA received Bactrim DS (sulfa-methoxazole 800 mg and trimethoprim 160 mg) twice daily for 7 days or, if they were allergic to cephalosporins with documented anaphylaxis, 300 mg of clindamycin 3 times daily for 7 days.

Procedure and Measures

Age, sex, body mass index (BMI), procedure type, risk factors for infection, infection within 1 year after the procedure, treatment for infection, and whether the patient was discharged with a prophylactic antibiotic were retrieved from the electronic medical record. Microbiology data were also obtained from medical records, and organisms were classified as resistant in accordance with the most recent Antibiotic Resistance Threats Report published by the Centers for Disease Control and Prevention (CDC) in 2019 [40]. Outpatient and emergency department visits and inpatient readmissions were reviewed to identify potential complications related to extended antibiotic therapy.

The Outcome of Interest

PJI meeting Musculoskeletal Infection Society criteria within 1 year after TJA was the outcome of interest in this study.

Data Analysis

Patients were categorized into 1 of 3 groups: group A, patients not at risk for PJI per protocol and therefore not given extended oral antibiotic treatment, group B, patients at risk for PJI per protocol but not given extended oral antibiotic treatment because our protocol was not in place, and group C, patients at risk for PJI who received extended oral antibiotic prophylaxis per protocol. Demographic characteristics and possible covariates, the prevalence of risk factors, prophylactic antibiotic administration, infection rates, and possible antibiotic-related complications were compared in the 3 groups. Minitab 19.1.1 (State College, PA) was used for data analysis. Group proportions were analyzed with the chi-square (X^2) test with Fischer’s P reported for 2 × 2 tables. The Mann-Whitney (W) and Kruskall Wallis (H) tests of medians were used to compare continuous variables because they were not normally distributed. Variables related to infection within one year with $P \leq .20$ were entered along with study group in binary logistic regression (BLR). The reference event for the dependent variable was occurrence of an infection within one year of surgery (ie, yes). The reference event for the predictor study group was group C. Reference events were yes or male for all other categorical variables and increasing increments of 10 for

continuous variables such as BMI. Initial models were refitted until the final model included only significant predictors. The Hosmer-Lemeshow test was used to assess model goodness of fit.

Source of Funding

The project described was supported by the Indiana University Health–Indiana University School of Medicine Strategic Research Initiative.

Results

The overall 1-year infection rate was 1.40% (54/3855) after primary TJA. The overall infection rates in groups A, B, and C were 1.29% (14/1082), 2.64% (23/870), and 0.89% (17/1903), respectively. Group C had a significantly lower rate of infection than group B ($P < .001$); however, the infection rate did not differ between group A and C patients ($P = .348$) with numbers available. Overall, the number needed to treat was 57 patients with extended antibiotics to prevent one PJI in high-risk patients.

Results are further presented separately by procedure type because the proportion of TKAs and THAs varied among the study groups ($X^2 = 24.097$, $P < .001$). Seventy-two percent (1690/2351) of patients who underwent TKA and 63% (942/1504) of patients who underwent THA had at least one risk factor for PJI ($X^2 = 36.243$, $P < .001$). Among at-risk patients, 42% (702) of the former and 40% (381) of the latter had more than one risk factor ($X^2 = 0.585$, $P = .591$). The proportion of patients who underwent TKA and THA categorized in study groups A, B, and C is shown in Table 2 ($X^2 = 24.097$, $P < .001$). For both procedures, group A had none of the protocol risk factors listed in Table 1. The prevalence of protocol risk factors in groups B and C is shown in Table 1.

The infection rate at one-year follow-up in patients who underwent TKA was 0.85% (20/2351). The highest rate of PJI was observed in group B at 1.78% (10/561), followed by 0.59% (7/1196) in group C, and 0.51% (3/594) in group A ($X^2 = 7.616$, $P = .022$). The one-year infection rate in patients who underwent THA was 2.26% (34/1504). Infection rates were 4.21% (13/309) for group B, 2.25% for group A (11/488), and 1.41% for group C (10/707) ($X^2 = 7.590$, $P = .022$). As shown in Table 2, for both procedures, distributions of demographics and covariates except for patient sex significantly differed based on study group ($P < .001$). The relationship between demographics and covariates and the occurrence of infection within one year is provided in Table 3. For TKA, only sex with a P value less than or equal to .20 qualified for entry into BLR along with study group as a potential predictor of infection within one year. For THA, BMI with a P value of .160 was entered into BLR along with study group.

For TKA, BLR modeling predicting infection in one year (yes/no) based on study group and sex (per Table 3) failed because of quasicomplete separation of data. Female patients (0.4%) had significantly lower one-year infection rates than male patients (1.8%, $X^2 = 12.632$, $P = .001$), and as shown in Figure 1, study group membership did not significantly affect infection rates for females ($X^2 = 3.280$, $P = .194$). One-year infection rates did significantly differ based on study group for male patients (Fig. 1), with the lowest rate of infection in

group A (0%, 0/210), followed by group C (1.57%, 6/380), and then group B (4.39%, 8/182; $X^2 = 10.811$, $P = .004$).

For THA, BLR modeling (Wald test $X^2 = 12.30$, df = 3, $P = .006$; goodness of fit $X^2 = 7.05$, $P = .531$) showed that study group ($X^2 = 8.10$, $P = .017$) and BMI ($X^2 = 5.31$, $P = .021$) were significant predictors of infection in one year. Compared with patients in group C, patients in group B were 3.4 times [95% confidence interval 1.4:7.8] more likely to develop PJI. The odds of PJI increased by 1.8 times [95% confidence interval 1.1:2.9] with increasing increments of 10 kg/m^2 BMI.

Four TKA and 12 THA infections were successfully treated with irrigation and debridement, and 16 TKAs and 22 THAs required resection and reimplantation. Organisms grown from PJI cultures in each group are in Table 4. Polymicrobial infection rates were 14.3% (2/14), 13.0% (3/23), and 11.8% (2/17) in groups A, B, and C, respectively. Drug-resistant infection rates were 7.1% (1/14), 0% (0/23), and 11.8% (2/17) in groups A, B, and C, respectively.

The influence of risk factors on infection rates is shown in Table 5. For THA, infection rates in patients with one or more (1.6% vs 4.2%, $P = .022$) or two or more (1.7% vs 7.2%, $P = .016$) risk factors were significantly lower in patients discharged on extended antibiotic prophylaxis. This also was the case for patients who underwent TKA with one or more risk factors (0.5% vs 1.8%, $P = .016$).

Of the 823 knee and hip patients whose BMI was ≥40, 1.3% discharged on antibiotics and 2.8% not discharged on antibiotics were diagnosed with infection within one year ($X^2 = 1.995$, $P = .216$). For the 746 diabetic patients, these rates were 0.8% and 3.7% ($X^2 = 8.600$, $P = .007$), respectively, and for the 321 patients who smoked, infection rates were 1.6% and 4.7% ($X^2 = 2.772$, $P = .164$), respectively.

Zero cases of *C. difficile* resulted from the extended antibiotic course, and only 6 patients (1 in group A, 3 in group B, and 2 in group C) were diagnosed with a complication that could possibly be related to antibiotic use, which resolved acutely. There were no cases of antibiotic drug toxicity observed.

Discussion

Postoperative antibiotics and their duration of administration are critical because of the bacterial burden and immune status of the patient after surgery, which can predispose the patient to infection. During the first 2 hours postoperatively, host defense mechanisms decrease the overall bacterial burden, while in the following 4 hours, the bacterial burden remains constant as bacteria are being killed by host defenses at the same rate of bacterial multiplication. These first 6 hours are referred to as the “golden period,” after which the bacteria multiply exponentially [41]. Postoperative antibiotics effectively decrease bacterial burden and work to extend the golden period. The hypothesis for our study protocol is that 7 days of antibiotics extends this golden period further for high-risk patients with compromising host factors.

We found that extended postoperative oral antibiotic prophylaxis for 7 days led to a statistically significant and clinically meaningful reduction in 1-year PJI rates for patients who are at high risk for infection. Overall, there was a 66.3% reduction in PJI rate after TJA in high-risk patients who received extended antibiotics (0.9% in group C compared with 2.6% in group B). Interestingly, high-risk patients who received extended antibiotics had an infection rate that was lower than that seen in low-risk patients (0.9% in group C compared with 1.3% in group A), although this was not statistically significant with numbers available. Each additional risk factor we studied appeared to increase the risk of PJI in our study population, which supports our protocol. Finally, we found zero cases of infection with *C. difficile*, and only 6 patients in total across all 3 groups were diagnosed with a complication that could possibly be related to an antibiotic, which resolved acutely with no long-term effects. Patients who received extended antibiotics and became infected also did not have a higher propensity for growing resistant organisms compared with other groups in our study, although the number of infections overall is small and precludes analysis. These findings support the efficacy and safety of using an extended antibiotic protocol for high-risk patients after TJA.

Data regarding the optimal duration of antibiotic prophylaxis after surgery have been conflicting, with low-level evidence suggesting that a single dose of antibiotics is as effective as multiple doses [42–50]. However, 2017 CDC guidelines recommended against the continuation of antibiotics postoperatively (after incision closure) after TJA [51]; this is concerning because the guidelines are based on only 6 orthopedic studies [47,52–56], 5 of which were published before 1991 and only 2 of which were TJA related. Data from other surgical specialties should not be extrapolated to orthopedic surgery particularly when hardware is involved, which has a high predilection for biofilm formation [57–60]. TJA is further unique in the use of various implant surfaces in prosthetic joints [61–63], including polyethylene which has a higher predilection for biofilm adhesion and formation [64–66]. Furthermore, the orthopedic studies cited in 2017 CDC guidelines did not use risk stratification analysis to examine low-risk and high-risk patients separately. In addition, an inconsistent definition of infection exists among the studies.

The most recent study supporting single-dose antibiotics was published in 2019 by Tan et al [50], after CDC guidelines were introduced. Their study demonstrated no difference in PJI rate between patients who received a single dose of antibiotics or multiple doses (0.60% vs 0.88%, $P = .064$). However, there were multiple variables that may not have been accounted for. Given the long study period, multimodal infection protocols that were incorporated into clinical practice were not accounted for and may have influenced the results. Patients in the single-dose group were healthier which may have led to an underestimation of PJI in that group, particularly because the single-dose group exhibited a lower rate of infection. Patients in the multiple-dose group were also more likely than the single-dose group to receive vancomycin. A study from the same institution previously reported that patients who received vancomycin prophylaxis alone had a 2-fold higher rate of infection than patients who received a first-generation cephalosporin alone [67]. Furthermore, because of the low-level evidence from this study and others in a recent meta-analysis [68], higher-quality contemporary studies are needed to evaluate the safety of shortened antibiotic prophylaxis after TJA and its effect on PJI before widespread implementation.

It is important to distinguish between the terminology of multiple doses and extended doses, the latter referring to antibiotics given beyond the traditional 24 hours of postsurgical IV antibiotics. Even though a few studies have shown no difference between single and multiple doses of antibiotics, only one other study [39] has explored extended antibiotics after primary TJA, which appears to lower the risk of infection compared with multiple doses of antibiotics in high-risk patients in our study.

Multiple studies support extended postoperative antibiotics for reducing reinfection rates in patients revised for PJI [34–38]. Most notably, in a multicenter randomized controlled trial, patients with chronic PJI who underwent two-stage revision and received a three-month course of oral antibiotics had significantly lower reinfection rates at 2-year follow-up than their counterparts who did not receive antibiotics (12.5% vs 28.6%, $P = .012$) [38]. The authors found side effects in patients who took doxycycline or ciprofloxacin, but no side effects were noted for patients receiving cefadroxil. Moreover, it is reasonable to assume that patients treated for PJI in Yang et al's [38] study had high-risk factors for infection at the time of primary TJA. Our study demonstrates that a short course of extended antibiotics in high-risk patients such as these may help prevent PJI after primary joint arthroplasty and avoid the associated burden of morbidity, mortality, and costs that come with PJI treatment.

The number needed to treat in our study was 57 high-risk patients with extended antibiotics to prevent one PJI, which would be very cost-effective in the long term. Although we were not able to perform a formal cost analysis, the costs of PJI are known to be multiple-fold higher than the cost of a primary TJA, ranging from $30,000 to over $100,000 in certain cases [6–12]. By comparison, the average manufacturer pricing for cefadroxil at a cost of $0.10 per 500 mg tablet amounts to $1.40 for a one-week supply (federal upper limit of $0.20 per tablet, or $2.80 for one week) [69,70]. Thus, 57 patients with a one-week supply would cost an average of $79.80, with a federal upper limit of $159.60, magnitudes lower than the cost of treating a single PJI.

Several institutions have implemented strict BMI or diabetic marker cutoffs before TJA, and thus, extended oral antibiotic prophylaxis may not apply to their patient populations. Furthermore, some surgeons and institutions are financially incentivized to select for healthier patients because of outcome-based reimbursement models [30–33]. However, many of these high-risk patients are unable to modify or optimize their medical comorbidities, and there is little evidence to support that optimization actually decreases infection risk, as seen in literature examining bariatric surgery for weight reduction, smoking cessation, and nasal colonization screening and treatment, among others [17–24]. Many of these patients seek care at other institutions, usually at academic or tertiary referral centers, after rejection by other centers. While there are certain comorbidities (such as severe cardiovascular compromise) that may preclude surgical intervention, denying elective surgery to patients on the basis of BMI or diabetes cutoffs attempts to mitigate risk at the expense of improving patient quality of life [71]. It is important to note that we do not advocate for extended oral antibiotics for all patients, but our findings suggest that there may be appropriate indications for extended antibiotic prophylaxis in high-risk patients.

Finally, we found a difference between men and women undergoing TKA, with women having a low infection rate regardless of study group. Sex differences in complications after TJA, including a higher likelihood of wound complications and surgical site infections in men, have been documented [72–76]. Despite few studies that have noted male sex as a risk factor for PJI after TJA [13,77,78], our observation of a 0.4% TKA infection rate in women and a 1.8% rate in men is compelling. Sex differences we could not account for may be responsible for this disparity. For example, men are more susceptible to peripheral arterial disease [79–84], which is commonly manifested in the lower extremities and is associated with infection risk [77,85,86]. The risk for infection is potentially higher in knees than in hips given the more distal aspect of the limb, and thus, peripheral vascular disease would be more impactful. Although high-risk women who underwent TKA and received extended antibiotics appeared to have a lower infection rate, we may have been underpowered to detect a statistical difference. Furthermore, given that high-risk women who received extended oral antibiotics in the THA group had a significant reduction in PJI rate, we believe it is still valuable to treat all high-risk women with this protocol.

Interpretation of our findings should be made relative to study limitations. The study was limited in its retrospective nature but utilized prospectively collected data which strengthened its accuracy. There were some factors that could not be accounted for because of the retrospective design, including malnutrition, preoperative anemia, cardiovascular disorders, excessive alcohol consumption, and depression, which have been shown to be risk factors for PJI [15,85,87]. Finally, we also could not capture patients who were treated for infection outside of our hospital system. This is unlikely, however, because all patients were seen by the operative surgeon at 4 weeks, 4 months, and 1 year postoperatively and were contacted by office staff if they missed their follow-up appointment. In our experience, most patients with signs of infection after primary TJA will contact their operative surgeon for assistance, and other hospitals are unlikely to accept patients with PJI after an operation performed elsewhere.

The 90-day PJI prevention results from our original study were upheld out to one year, and in an expanded sample size, demonstrating a statistically significant and a clinically meaningful reduction in 1-year infection rates. In fact, the PJI rate in high-risk patients who received antibiotics was less, but not statistically different, than the rate seen in low-risk patients. A one-week supply of extended antibiotics is also cost-effective with a number needed to treat 57 patients to prevent one PJI. Moreover, as evidenced by the number of high-risk patients in our study as a tertiary referral center, extended oral antibiotics may mitigate the potential incentive of outcome-based reimbursement models to select for healthier patients, distributing the burden of high-risk patients among tertiary referral centers and private hospitals.

In conclusion, extended oral antibiotic prophylaxis may be a simple, safe, and cost-effective measure to counteract poor host factors, which can be difficult to modify or optimize, to reduce PJI rates at 1 year postoperatively. Further study with a multicenter randomized control trial is needed to further validate this protocol and our results, as well as quantify any potential adverse consequences such as antimicrobial resistance.

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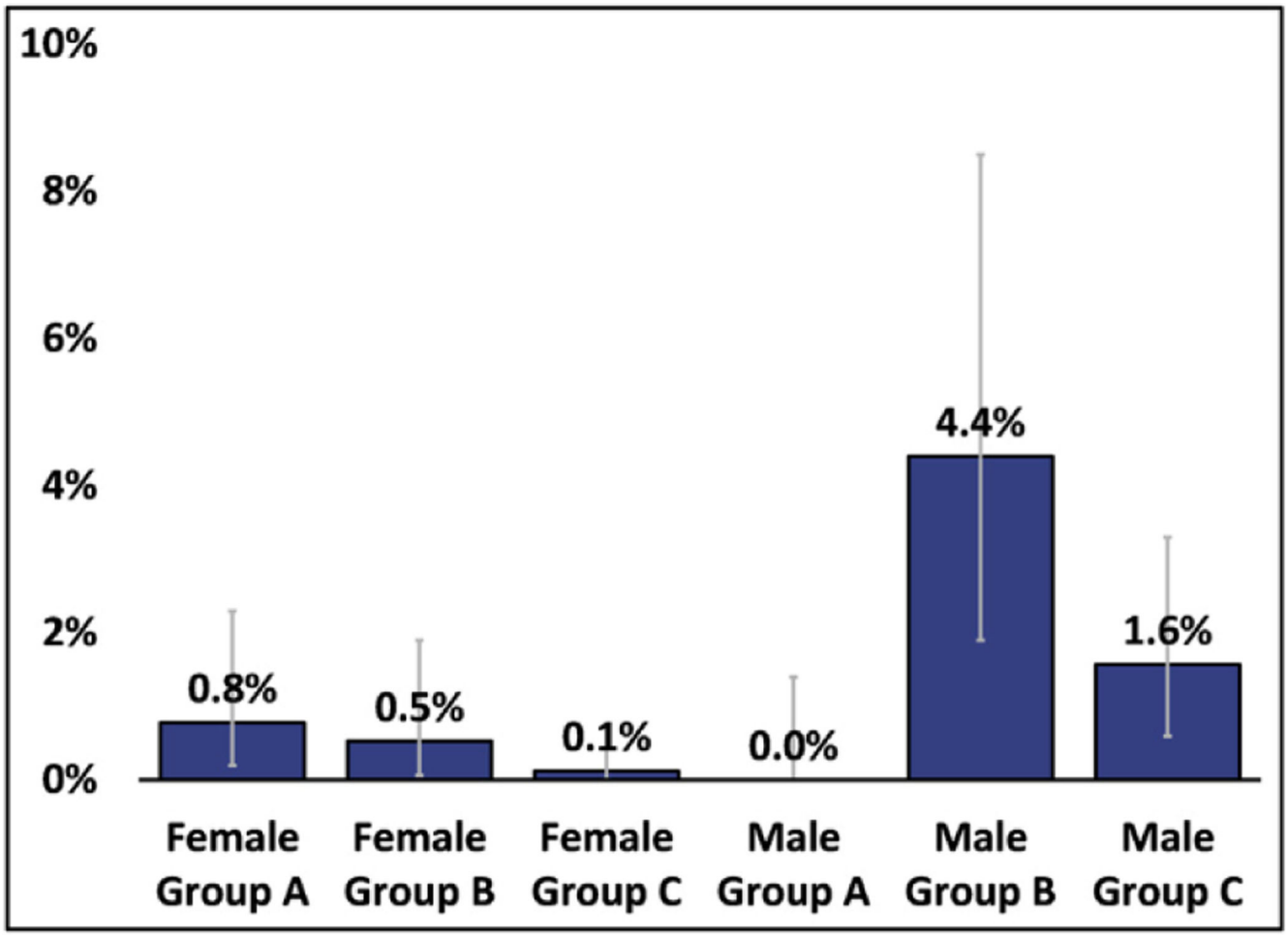

Fig. 1.

One-year TKA infection rate by study group and sex ($P = .194$ for females and $P = .004$ for males). Gray bars depict 95% confidence intervals for sample proportions. TKA, total knee arthroplasty.

Table 1

Distribution of Risk Factors in Groups B and C Based on Procedure Type[a].

Risk Factor	TKA				THA			
	% in Group B	% in Group C	X^2	*P*	% in Group B	% in Group C	X^2	*P*
% BMI ≥35	62.6	66.0	1.941	.164	42.7	51.2	6.195	**.014**
% diabetes mellitus	25.3	30.2	4.436	**.036**	23.3	24.2	0.093	.811
% active smoker	11.4	7.0	9.518	**.003**	20.7	15.4	4.267	**.046**
% chronic kidney disease	13.4	14.6	0.437	.557	12.9	14.1	0.260	.692
% autoimmune disease[b]	11.2	11.8	0.116	.750	10.7	11.6	0.181	.747
% nasal colonization with MRSA and/or MSSA[c]	14.1	23.8	20.509	**<.001**	22.8	26.1	1.250	.269
% other[d]	0.2	5.5	29.690	**<.001**	0.0	10.5	34.883	**<.001**

BMI, body mass index; TKA, total knee arthroplasty; THA, total hip arthroplasty.

Bolded values indicate a significant difference.

[a]Group B = at risk for infection, extended antibiotic prophylaxis not given; group C = at risk for infection, extended antibiotic prophylaxis given.

[b]Includes rheumatoid/psoriatic/inflammatory arthritis, systemic lupus erythematosus, inflammatory bowel disease/ulcerative colitis/Crohn's disease, multiple sclerosis, psoriasis. Grave's disease/ hypothyroidism, Hashimoto's/thyroiditis disease, myasthenia gravis, vasculitis, celiac disease, pernicious anemia, vitiligo, scleroderma/systemic sclerosis, Addison's disease/adrenal hormone insufficiency, Sjögren's/sicca syndrome.

[c]MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*. Nasal colonization with MRSA and/or MSSA was unknown for 39 TKAs and 24 THAs.

[d]Includes history of sepsis, hepatitis C, chronic recurrent cystitis, stasis dermatitis, traumatic catherization with hematuria, and patients who underwent surgery within 3 mo after cortisone intra-articular injection.

Table 2

Demographics and Covariates by Study Group for TKA and THA[a].

Procedure Demographic/Covariate	Group A	Group B	Group C	Statistic	*P*
TKA					
N (%)	594 (25.3)	561 (23.8)	1196 (50.9)		
% female	64.6	67.6	68.2	$X^2 = 2.630$	.307
Median age in years	67.9	65.4	64.9	H = 51.81	**<.001**
Median BMI in kg/m^2	29.0	36.5	37.0	H = 592.85	**<.001**
THA					
N (%)	488 (32.4)	309 (20.6)	707 (47.0)		
% female	58.8	60.5	60.1	$X^2 = 0.293$	.864
Median age in years	66.8	64.6	64.6	H = 18.24	**<.001**
Median BMI in kg/m^2	28	33	35	H = 249.49	**<.001**

BMI, body mass index; TKA, total knee arthroplasty; THA, total hip arthroplasty.

Bolded values indicate a significant difference.

[a]Group A = not at risk for infection, extended antibiotic prophylaxis not given; group B = at risk for infection, extended antibiotic prophylaxis not given; group C = at risk for infection, extended antibiotic prophylaxis given.

Table 3

Relationship Between Demographics, Covariates, and Infection Within One Year by Procedure Type.

Procedure Demographic/Covariate	Infection Within One Year		Statistic	*P*
	Yes	No		
TKA				
% female/male	0.4/1.8	99.6/98.2	$X^2 = 12.632$	**.001**
Median age in years	66.4	65.9	W = 2,742,176.5	.761
Median BMI in kg/m^2	32.1	34	W = 2,742,443.5	.694
THA				
% female/male	2.5/2.0	97.5/98.0	$X^2 = 0.352$	.600
Median age in years	66.8	65.3	W = 1,105,862.5	.901
Median BMI in kg/m^2	33	31	W = 1,102,688.5	.160

BMI, body mass index; TKA, total knee arthroplasty; THA, total hip arthroplasty. Bolded values indicate a significant difference.

Table 4

Organisms Cultured From PJI Cases by Study Group[a].

Group A	Group B	Group C
Beta hemolytic Streptococci, group C	Coagulase-negative Staphylococcus	Beta hemolytic Streptococci, group C
Coagulase-negative Staphylococcus	Coagulase-negative Staphylococcus	MSSA
Staphylococcus lugdunensis	MSSA	[c]MRSA
[b] [c]MRSA; *Proteus mirabilis*	*Serratia marcescens*	[b]*Pseudomonas aeruginosa*; Enterococcus species
MSSA	MSSA	MSSA
MSSA	MSSA	*P aeruginosa*
Enterobacter aerogenes	MSSA	Coagulase-negative Staphylococcus
P aeruginosa	MSSA	Culture negative
MSSA	MSSA	Culture negative
Coagulase-negative Staphylococcus	MSSA	MSSA
Coagulase-negative Staphylococcus	Culture negative	Culture negative
Mycobacterium fortuitum	MSSA	[b]*P mirabilis*; Enterococcus species
[b]Coagulase-negative Staphylococcus; *S lugdunensis*	*P aeruginosa*	MSSA
Culture-negative	*P aeruginosa*	Peptostreptococcus species
	[b]MSSA; *Enterobacter cloacae; S marcescens*	Beta hemolytic Streptococci, group G
	MSSA	*Staphylococcus epidermidis*
	[b]Coagulase-negative Staphylococcus; *Morganella morganii*	[c]MRSA
	[b]MSSA, *E. Coli*	
	MSSA	
	Corynebacterium species	
	S marcescens	
	MSSA	
	MSSA	

MSSA Methicillin-sensitive *Staphylococcus aureus*; MRSA = Methicillin-resistant *S aureus*.

[a]Group A = not at risk for infection, extended antibiotic prophylaxis not given; group B = at risk for infection, extended antibiotic prophylaxis not given; group C = at risk for infection, extended antibiotic prophylaxis given.

[b] Polymicrobial infection.

[c] Considered resistant bacteria in accordance with CDC Antibiotic Resistance Threats 2019 Report [40].

Table 5

Rate of Infection Within One Year Based on Number of Risk Factors and Receipt of Extended Oral Antibiotic Prophylaxis by Procedure.

Procedure	Extended Oral Antibiotics = Yes		Extended Oral Antibiotics = No		X^2	P [a]
Number of Risk Factors	**No.**	**%**	**No.**	**%**		
THA						
≥1 risk factors	10/633	1.6	13/309	4.2	6.017	**.022**
≥2 risk factors	5/298	1.7	6/83	7.2	7.135	**.016**
≥3 risk factors	3/68	4.4	1/18	5.6	*b*	
TKA						
≥1 risk factors	6/1130	0.5	10/560	1.8	6.286	**.016**
≥2 risk factors	5/535	0.9	4/167	2.4	2.145	.228
≥3 risk factors	0/144	0.0	2/40	5.0	*b*	

TKA, total knee arthroplasty; THA, total hip arthroplasty.

[a] Bolded values indicate a significant difference.

[b] X^2 approximation invalid due to low expected cell counts.

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