

# Single Prophylactic Antibiotic Dose for Total Knee Arthroplasty Resulting in No Increased Risks in Prosthetic Joint Infection

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**INTRODUCTION:** There has been conflicting evidence whether extended oral antibiotic prophylaxis can reduce prosthetic joint infection (PJI) after total knee arthroplasty (TKA). In this study, we aim to investigate the efficacy of four common antibiotic prophylactic regimens to prevent PJI.

**METHODS:** In this observational study, 8,676 patients undergoing outpatient TKA between 2017-2019 were examined. Patients receiving single-dose prophylactic antibiotic (n= 2,224) were compared to patients with multiple-dose (n= 3,617), multiple types (n= 2,468), and extended oral prophylaxis (n= 367). Patients who developed 90-day and one-year PJI were identified. Additionally, we compared the PJI rate between those with and without extended oral prophylaxis among selected high-risk patients. Multivariate regression models were performed to adjust for potential confounders.

**RESULTS:** Overall, 75 patients (0.9%) developed 90-day PJI. Compared to patients with single-dose prophylaxis, those with multiple-dose were not associated with a lower PJI risk (OR= 1.50, 95% CI [0.74, 3.03]); neither were patients with multiple types (OR= 1.90, 95% CI [0.93, 3.89]) nor patients with extended oral prophylaxis (OR= 1.82, 95% CI [0.58, 5.89]). Findings were similar for high-risk patients, where extended oral prophylaxis was not associated with a decreased PJI rate when compared to no oral prophylaxis (OR= 1.60, 95% CI [0.49, 5.28]).

**DISCUSSION AND CONCLUSION:** More than a single dose of prophylactic antibiotic was not associated with a reduced PJI risk after TKA. Similarly, for TKA patients with high risks of infection, extended oral prophylaxis did not decrease the risk.

Table 1. Characteristics of patients undergoing total knee arthroplasty (TKA) by prophylactic regimen

Variable	Single dose (n=2224)	Multiple dose (n=3617)	Multiple types (n=2468)	Extended oral (n=367)	P-value
Female, %	51.8 (23.2)	51.8 (23.2)	51.8 (23.2)	51.8 (23.2)	0.92
Age, mean (SD)	65.1 (10.7)	65.1 (10.7)	65.1 (10.7)	65.1 (10.7)	0.92
Diabetes, %	10.2 (4.6)	10.2 (4.6)	10.2 (4.6)	10.2 (4.6)	0.92
Chronic kidney disease stage 3-5, %	1.2 (0.5)	1.2 (0.5)	1.2 (0.5)	1.2 (0.5)	0.92
Substance abuse, %	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.92
Smoking, %	14.1 (6.3)	14.1 (6.3)	14.1 (6.3)	14.1 (6.3)	0.92
Malabsorbtion of MRSA or MSSA, %	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.92
Infusion within 30 days prior to TKA, %	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.92

Table 2. Adjusted analysis on the risk of 90-day prosthetic joint infection among all patients (N=8676)

Variable	OR (95% CI)	P-value
<b>Antibiotic regimens</b>		
Single dose of IV antibiotics*	1 (reference group)	-
Multiple doses of the same type IV antibiotics	1.50 (0.74, 3.03)	0.26
Multiple types** of IV antibiotics	1.90 (0.93, 3.89)	0.08
Both IV and extended oral antibiotics**	1.82 (0.58, 5.89)	0.30
<b>Age</b>		
<55 years	1 (reference group)	-
55-65 years	0.79 (0.48, 1.29)	0.35
>65 years	0.45 (0.26, 0.80)	0.005
<b>Gender</b>		
Male	1 (reference group)	-
Female	0.41 (0.26, 0.69)	<0.001
<b>History of comorbidities</b>		
Diabetes with hypoglycemia	0.75 (0.36, 1.52)	0.44
Chronic kidney disease	1.31 (0.71, 2.50)	0.37
Substance abuse	1.00 (1.04, 0.97)	0.68
Malabsorbtion of MRSA or MSSA	2.00 (1.19, 3.33)	0.008
Infusion within 30 days prior to TKA	1.11 (0.44, 2.79)	0.77
Smoking	2.06 (0.84, 11.23)	0.17

\*Reference: OR, Odds ratio; CI, Confidence interval; IV, Intravenous; BMI, Body mass index; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.  
 \*\*Prophylactic IV antibiotics examined in the study included Cefazolin, Cefuroxime, Vancomycin, and Clindamycin.  
 \*\*\*Patients in this group and different types of IV antibiotics concurrently, regardless of dose.  
 \*\*\*\*Prophylactic oral antibiotics examined in the study included Cefadroxil, Cefaclor, and Clindamycin, which prescribed within 30 days before or 7 days after TKA.

Table 3. Characteristics of high-risk patients undergoing total knee arthroplasty (TKA), by prophylactic regimens

Variable	Overall high risk patients (N=3333)	Patients without oral antibiotics (N=148)	Patients with oral antibiotics** (N=3185)	P-value
Female, %	51.1 (25.2)	50.2 (25.2)	51.2 (25.2)	0.37
Age, mean (SD)	59.1 (8.4)	59.2 (8.2)	59.1 (7.3)	<0.01
<b>History of comorbidities</b>				
Diabetes with hypoglycemia, %	312 (15.4%)	400 (15.4%)	22 (0.9%)	0.87
Chronic kidney disease stage 3-5, %	4 (0.2%)	8 (0.3%)	6 (0%)	0.84
Substance abuse, %	1 (0.0%)	1 (0.4%)	0 (0%)	0.84
Smoking, %	119 (4.5%)	114 (4.5%)	4 (0.1%)	0.86
Malabsorbtion of MRSA or MSSA, %	119 (4.5%)	114 (4.5%)	4 (0.1%)	0.85
Infusion within 30 days prior to TKA, %	112 (4.2%)	107 (4.2%)	5 (0.2%)	0.85

\*Reference: OR, Odds ratio; CI, Confidence interval; BMI, Body mass index; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.  
 \*\*High risk patients were defined as having any of the known risk factors for prosthetic joint infection, including type 2 Diabetes Mellitus, chronic kidney disease, end-stage renal disease, substance abuse, malabsorbtion, smoking, and oral colonization of MRSA or MSSA, and infection within 30 days prior to TKA.  
 \*\*\*Prophylactic oral antibiotics examined in the study included Cefadroxil, Cefaclor, and Clindamycin, which prescribed within 30 days before or 7 days after TKA.

Table 4. Adjusted analysis on the risk of 90-day prosthetic joint infection among high-risk\* patients (N=3333)

Variable	OR (95% CI)	P-value
<b>Antibiotic regimens</b>		
Without oral antibiotics	1 (reference group)	-
With oral antibiotics**	1.60 (0.96, 2.78)	0.44
<b>Age</b>		
<55 years	1 (reference group)	-
55-65 years	0.71 (0.37, 1.35)	0.22
>65 years	0.52 (0.19, 1.43)	0.21
<b>Gender</b>		
Male	1 (reference group)	-
Female	0.48 (0.25, 0.89)	0.02
<b>Number of risk factors</b>		
1 risk factor	1 (reference group)	-
2 risk factors	1.14 (0.21, 2.31)	0.74
3 risk factors	0.86 (0.06, 8.36)	0.36

\*High risk patients were defined as having any of the known risk factors for prosthetic joint infection, including type 2 Diabetes Mellitus, chronic kidney disease, end-stage renal disease, substance abuse, malabsorbtion, smoking, and oral colonization of MRSA or MSSA, and infection within 30 days prior to TKA.  
 \*\*Prophylactic oral antibiotics examined in the study included Cefadroxil, Cefaclor, and Clindamycin, which prescribed within 30 days before or 7 days after TKA.