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Factors affecting the duration of antibiotic use due to surgical site inflammation after complication-free classical total knee arthroplasty

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Abstract

We researched on the factors affecting the duration of antibiotic use due to surgical site inflammation after complication-free classical total knee arthroplasty (TKA).

Four hundred and eighty-nine cases who underwent primary TKA performed by 1 surgeon from January 2015 to December 2018 were enrolled. Including the day of operation, first-generation cephalosporin was injected intravenously for 3 days for antimicrobial prophylaxis. At the third postoperative day, we inspected the surgical wound for any signs of inflammation. If there were any signs of redness, pain, heatness, or swelling, which are the cardinal signs of superficial incisional surgical site infection defined by the Centers of Disease Control (CDC), additional antibiotics were injected until the symptoms of surgical site inflammation improved. We presumed that the duration of antibiotic use was affected by factors including gender, age, body mass index, whether operating on both legs or one leg, predisposing diabetes mellitus, preoperative glomerular filtration rate, preoperative serum albumin level, prior history of anticoagulant usage including anti-platelet agents, allogenic blood transfusion during admission, and total operative time.

Average duration of intravenous antibiotic use in 489 cases was 5.73 ± 4.03 days. Pearson correlation analysis showed significant correlation ($P < .01$) between operative time and duration of antibiotic use due to surgical site inflammation. In univariate analysis, total operative time and transfusion were factors affecting the duration of antibiotic use due to surgical site inflammation (<6 days or ≥6 days). Multivariate analysis of age, gender, body mass index, staged bilateral TKA, diabetes mellitus, preoperative glomerulus filtration rate, preoperative albumin level, prior history of anticoagulant usage, allogenic blood transfusion during admission, and total operative time revealed that longer operative time was related to higher likelihood of antibiotic use for >6 days during admission.

When prophylactic antibiotics are prescribed, surgeons must note that signs of superficial incisional surgical site inflammation after classical complication free TKA may manifest more often in patients with longer operative time.

Abbreviations: BMI = body mass index, GFR = glomerulus filtration rate, TKA = total knee arthroplasty.

Keywords: prophylactic antibiotics, surgical site inflammation, total knee arthroplasty

1. Introduction

Infection after primary total knee arthroplasty (TKA) occurs approximately in 1% of all cases and may cause critical complications.[1,2] Surgeons put a lot of effort to prevent some of the complications by using prophylactic antibiotics or reducing postoperative transfusion. Nowadays, although there is no doubt on using prophylactic antibiotics,[3] there are no "totally-agreed" guidelines on the duration of antibiotic use. The American Academy of Orthopedic Surgeons (AAOS) and the Musculoskeletal Infection Society (MSIS) recommends to stop the use of prophylactic antibiotics within 24 hours after surgery.[4] However, physicians tend to prescribe longer than such recommendations in concern of postoperative infection after TKA. In South Korea, the average duration of prophylactic antibiotics in 2015 and 2016 were 8.04 and 7.79 days, respectively.[5] The fear that inflammation at the surgical site might cause infection may be one the reasons why many surgeons prescribe prophylactic antibiotics longer than it is recommended. There are numerous studies on factors that triggers postoperative infection of TKA.[6–8] However, very few is known about the factors affecting the duration of antibiotic use due to surgical site inflammation after complication-free classical TKA.

We presumed that gender, age, body mass index (BMI), whether operating on both leg or one leg, predisposing diabetes mellitus, preoperative glomerulus filtration rate (GFR), preoperative serum albumin level, prior history of anticoagulant usage, allogenic transfusion during admission, and total operative time affects the duration of antibiotic use.[9–11] Thus, we tried to figure out the relationship between such various factors and surgical site inflammation.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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We hypothesized that among the factors, allogenic transfusion and longer operative time increases the duration of antibiotic use after classical complication free TKA. This study was approved by the Institutional Review Board (CR-20-006).

2. Materials and methods

Patients who underwent primary TKA performed by 1 surgeon from January 2015 to December 2018 were screened for eligibility. Subjects undergoing revision TKA, subjects with post-infectious arthritis, and post-traumatic arthritis were excluded from the study. Total subjects were 523 cases. Thirty two cases which early surgical complications (hematoma, pneumonia, and etc . . .) occurred were excluded. Two cases were excluded due to reoperation after infection within a year after the first surgery. A total of 489 cases were included to the study. Baseline characteristics of the patients are descripted in Table 1.

All operations were held by one surgeon using posterior cruciate ligament substituting (PS) design implants. Indwelling catheters were inserted at the surgical site in all patients, and catheters were all removed at the first or second postoperative date depending on the amount of blood drainage. If the patient was using an anti-platelet agents or anti-coagulants, such drugs were discontinued for 5 days before the operation after consultation to the relevant departments. Anticoagulants were continued soon after the operations were performed. If patients had underwent TKA surgery on both knees during a single admission period, the second operation was performed 2 weeks after from the first surgery.

2.1. Use of antibiotics

Antibiotic prophylaxis with first-generation cephalosporin was continued for 3 days including the operation day, according to our medical center's clinical guideline. At the third postoperative day, we examined the surgical wound. If there were any signs of redness, pain, heat, or swelling, which are signs of superficial incisional surgical site infection of the CDC,[12] we documented such signs in the progress note and prescribed additional antibiotics and continued it until the signs of surgical site inflammation improved.

2.2. Analysis of transfusion

We measured the frequency of transfusion after operation within the admission period (2 weeks). According to American Blood Bank Guideline,[13] patients with hemoglobin level of <8 g/dL underwent blood transfusion while also considering their clinical symptoms.

Table 1

Basic information of the patients.

Variables		Values
Age, y		72.44 ± 7.55
Gender (female: male)		426: 63
Body mass index, kg/m^2		25.41 ± 3.43
Preoperative GFR (mL/min/1.7 m^2)		84.71 ± 16.61
Preoperative albumin, g/dL		4.15 ± 0.35
Total operative time, min		87.96 ± 12.64
Sites of operation	One side	225 (225 person)
	Both sides	264 (132 person)
Diabetes melitus	Yes	107 (21.9%)
	No	382 (78.1%)
Transfusion	Yes	182 (37.2%)
	No	307 (62.8%)
Anticoagulant	Yes	160 (32.7%)
	No	329 (67.3%)

2.3. Statistical analysis

Pearson correlation analysis was carried out to assess the relationship between the duration of antibiotic use and age, BMI, preoperative GFR, preoperative albumin level, and total operative time. Also, *t* test was performed in order to measure the correlation between the gender, whether operating on both or one leg, predisposing diabetes mellitus, use of anti-platelet or coagulant agents, transfusion during admission, and the duration of antibiotic use. The chi-square test was used to analyze the relationship between antibiotic use of ≥ 6 days and gender, whether operating on both or 1 leg, predisposing diabetes mellitus, use of anti-platelet or coagulant agents, transfusion during admission. Regression analysis was used to assess the association between several factors and duration of antibiotics (<6 days or ≥ 6 days). *P*-value of $<.05$ was considered to indicate statistical significance. Analyses were carried with IBM SPSS Statistics ver. 19 (IBM Co., Armonk, NY).

3. Results

The average duration of intravenous antibiotic use in 489 cases was 5.73 ± 4.03 days.

3.1. Relationship between subject's age, BMI, preoperative GFR, preoperative albumin level, total operative time, and duration of antibiotic use

Pearson correlation analysis showed significant correlation ($P < .01$) between operative time and the duration of antibiotic use. Age, BMI, preoperative GFR, and preoperative albumin level did not show significant correlation with the duration of antibiotic usage (Table 2).

3.2. Differences in the duration of antibiotic use depending on subject's gender, 1 or 2 leg operation, predisposing diabetes mellitus, prior history of anti-platelet or anticoagulant use, and blood transfusion during admission

The average antibiotic use was 5.45 ± 3.92 days in the group with no transfusion, while the group with transfusion was 6.21 ± 4.16 days. The *t* test was used for this comparison and showed statistical significance ($P = .04$). Also, the group without prior history of anti-platelets or anti-coagulants showed 5.47 ± 3.81

Table 2

Pearson analysis between total operative time, age, BMI, preoperative GFR, and preoperative albumin level and the duration of antibiotic usage.

	Correlation coefficient	*P* value
Total operative time	0.14	<.01
Age	0.03	.53
Body mass index	−0.09	.06
Preoperative GFR	−0.06	.20
Preoperative albumin level	−0.07	.13

BMI = body mass index, GFR = glomerulus filtration rate.

Table 3

Difference in duration of antibiotic use depend on anti-platelet or coagulant agents, and transfusion during admission.

		Duration of antibiotics, d	*P* value
Transfusion	No	5.45 ± 3.92	.04
	Yes	6.21 ± 4.16	
Anticoagulant	No	5.47 ± 3.81	.04
	Yes	6.28 ± 4.40	

days of antibiotic use, while the group with prior history of anti-platelets or anti-coagulants had 6.28 ± 4.40 days in average. There was also a significant difference between the 2 groups ($P = .04$) (Table 3).

3.3. Relationship between antibiotic use of 6 days or longer with gender, whether operating on both or 1 leg, predisposing diabetes mellitus, use of anti-platelets or anti-coagulants, transfusion during admission

Average duration of intravenous antibiotic use in 489 cases was 5.73 ± 4.03 days. We divided the cases into 2 groups, based on the 6-day period of use of antibiotics. The Chi-square test showed significant correlation between transfusion during admission and antibiotic use of 6 days or longer (Table 4).

3.4. Factors affecting duration of antibiotics (<6 days or ≥6 days)

In univariate analysis, total operative time and transfusion were factors affecting duration of antibiotics (<6 days or ≥6 days). Multivariate analysis of age, gender, BMI, diabetes mellitus, preoperative GFR, preoperative albumin level, use of anti-platelets or anticoagulants, allogenic transfusion during admission, and total operative time revealed that longer operative time was related to higher likelihood of antibiotic use for >6 days during admission (Table 5).

3.5. Cut-off time of total operative time for duration of antibiotics (<6 days or ≥6 days)

The cut-off time of operative time for duration of antibiotics (<6 days or ≥6 days) was obtained through receiver operating characteristic (ROC) curve, and the value of cut-off time was found to be 89 minutes. As a result of ROC analysis, the area under the curve (AUC) value was 0.592, with a 95% confidence interval of 0.55 to 0.64 and a *P*-value of .01. Also, the sensitivity and specificity were 49.1 and 68.3, respectively (Fig. 1).

4. Discussion

The National Evidence-based Healthcare Collaborating Agency has analyzed 150,000 patients who had primary TKA in between 2008 and 2015 in use of prophylactic antibiotic use.[5] There was no significant difference in the occurrence rate of surgical site infection between the group who followed the international guideline-antibiotic use of within 2 days- and the group who did not follow. However, surgeons are still using antibiotics longer than the guideline in concern of serious postoperative infection.[14]

In this study, we have proved that longer operative time has led to increased occurrence of signs of superficial incisional surgical site inflammation, which resulted in longer use of antibiotics. We think that longer operative time may cause more trauma during surgery and thus lead to postoperative inflammation at the surgical site. Numerous studies have already shown that longer operative time, use of anti-thrombotic agents, and transfusion during admission period are some of the factors which increase postoperative infection.[15–17] Especially, transfusion is thought to be the major factor and surgeons try to lower blood loss by

Table 4

Chi-square test between 6 days or longer use of antibiotic and use of anti-platelet or coagulant agents, transfusion within admission.

		Duration of antibiotics			
		<6 days	≥6 days	Total	*P* value
Transfusion	No	214	93	307	.02
	Yes	108	74	182	
	Total	322	167	489	

Table 5

Multiple variables logistic regression analysis, which analyzed factors affecting duration of antibiotics (<6 days or ≥6 days).

	Crude			Adjusted*		
Variable	OR	95% CI for OR	*P* value	OR	95% CI for OR	*P* value
Operative time	1.02	1.01/1.04	.01	1.03	1.01/1.04	.01
Transfusion (yes)	1.58	1.08/2.31	.02	1.41	0.93/2.14	.11
Age	1.01	0.99/1.04	.37	1.00	0.98/1.04	.73
Gender (male)	0.96	0.55/1.68	.88	0.85	0.47/1.52	.58
BMI	0.95	0.90/1.01	.09	0.97	0.91/1.03	.28
DM (yes)	0.70	0.45/1.12	.13	0.68	0.42/1.12	.13
GFR	1.00	0.99/1.01	.45	1.00	0.98/1.01	.52
Albumin	0.69	0.41/1.17	.17	0.67	0.39/1.15	.15
Anticoagulant (yes)	1.25	0.84/1.85	.28	1.03	0.82/1.91	.30

BMI = body mass index, CI = confidence interval, GFR = glomerulus filtration rate, OR = odds ratio.

* Adjusted by age, gender, BMI, diabetes melitus, preoperative GFR (glomerulus filtration rate), preoperative albumin level, use of anti-platelet or coagulant agents, allogenic transfusion during admission period, and total operative time.

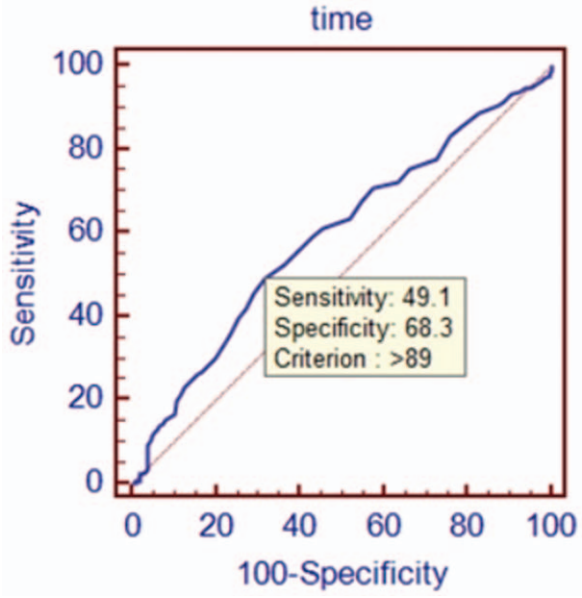

Figure 1. The cut-off time of operative time for duration of antibiotics (<6 days or ≥6 days).

using intraoperative tourniquets, tranexamic acid, and any others they could do.[18]

As said before, there are few studies on factors that increase the duration of antibiotic use. If surgeons are aware of factors that could increase the duration of antibiotic use before performing the surgery, they could manage such factors and use less antibiotics.

There are various guidelines of using prophylactic antibiotics.[4,5] However, most of the guidelines recommend the use of postoperative antibiotics for <2 days, and such is also recommended for surgeons in South Korea. However, the average duration of postoperative antibiotics in South Korea was 8.87 days in 2008 and 7.79 days in 2016.[5] Statistics display the tendency of the duration of antibiotic use after TKA to decrease, but it is still apart from the international guideline. To close the gap, South Korean surgeons must reveal the factors that could increase the duration of antibiotic use due to surgical site inflammation.

This study has some limits. Firstly, this is a retrospective study. Secondly, the signs of superficial incisional surgical site infection of CDC which were checked on the third postoperative day could be subjective and vary by different surgeons who examine them. Thirdly, since this study was on patients without complications after TKR, we did not analyze the factors in relationship with patients with postoperative complications. In our study, among 523 cases, postoperative infection which required revision surgery occurred in 2 cases. Further research with larger case numbers would be needed for more detailed results about the relationship between several factors and the occurrence of postoperative complications. Fourthly, among the subjects, the proportion of women is much higher than that of men, which may cause bias. Among TKAs conducted in Korea, the proportion of women actually corresponds to 9 times that of men.[19]

5. Conclusion

When prescribing prophylactic antibiotics, surgeons must note that signs of superficial incisional surgical site inflammation after classical complication free total knee arthroplasty occurs more in patients with longer operative time.

Author contributions

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