

Impact of a change in duration of prophylactic antibiotics on infectious complications after radical cystectomy with a neobladder

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Abstract

A profound number of prophylactic antibiotics are used after radical cystectomy with an ileal orthotopic neobladder (RCIONB) despite a negative effect of infection control. We investigated the impact of short-term prophylactic antibiotic use on infectious complications after RCIONB.

We retrospectively reviewed data from 287 patients who underwent RCIONB for bladder cancer between 2012 and 2016 at a tertiary hospital. The patients were divided into 2 groups according to the pattern of prophylactic antibiotics (185 patients in a long-term group, 25-day use of 3-staged multiple antibiotics versus 102 patients in a short-term group, 24-hour use of cefotetan). The onset of complications, including bacteriuria, febrile urinary tract infection (FU), and bacteremia, and the microorganisms responsible for infections were compared between the groups. Of all 287 patients, bacteriuria, FU, and bacteremia were identified in 177 (61.7%), 85 (29.6%), and 18 (6.3%) patients, respectively. Bacteriuria was identified more frequently in the short-term group (49.2% vs 84.3%, $P < .001$). However, the rates of FU within 60 days of surgery were similar in both groups (28.6% vs 28.4%, $P = .969$). The rate of FU was not significantly different between the 2 groups. There was no significant difference in the rate of patients with bacteremia (5.4% vs 7.8%, $P = .415$). The most frequent microorganisms seen in bacteriuria were *Enterococcus faecium* and *Enterococcus faecalis*, in the long-term and short-term group, respectively. Antibiotic-resistant *Enterococcus* species were more frequently present in the long-term group.

Short-term use of prophylactic antibiotics is effective for preventing urinary tract infections after RCIONB and decreasing colonization with multi-drug-resistant organisms.

Abbreviations: 3GC = third-generation cephalosporin, CDAD = *Clostridium difficile*-associated diarrhea, FU = febrile urinary tract infection, pre-Op = preoperative, post-Op = postoperative.

Keywords: antibiotic prophylaxis, cystectomy, urinary bladder neoplasm, urinary tract infections

1. Introduction

Bladder cancer is the sixth most common cancer in males worldwide,^[1] and the number of new cases is increasing in South Korea annually.^[2] Radical cystectomy (RC) is the standard treatment for muscle-infiltrating or recurrent, high-risk non-muscle-invasive bladder cancer. After RC, various urinary diversion techniques are used, including ileal conduit urinary

diversion and ureterocutaneostomy,^[3] and an ileal orthotopic neobladder (IONB) is increasingly used as a urinary diversion method because of its advantages with regard to quality of life.^[4,5]

However, infectious complications are among the major concerns after RC with an IONB.^[6,7] Infectious complications are more frequent after IONB surgery than other urinary diversions for several reasons. First, an IONB is reconstructed using the ileum, which has higher levels of bacteria and mucus compared to the urinary bladder. Second, an anti-reflux mechanism is absent from an IONB. Third, long-term use of a urinary catheter after surgical treatment facilitates colonization of the urinary system by bacteria. Therefore, many surgeons use great deal of prophylactic antibiotics during RC with an IONB.^[8–11] Although the efficacy of short-term prophylactic antibiotic use has been proven in various surgeries,^[12] there is little evidence regarding its efficacy in urological surgery. Therefore, we evaluated the impact of short-term prophylactic antibiotic use compared to long-term prophylactic antibiotic use on infectious complications after RC with an IONB.

2. Patients and methods

2.1. Study populations and prophylactic antibiotic regimen

We retrospectively collected the medical records of 315 patients undergoing RC with an IONB for bladder cancer from January 2012 through December 2016 at a single tertiary university-affiliated hospital. We excluded patients undergoing RC for other

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reasons, including rectal cancer or uterine cancer invasion to the bladder ($n=9$), and those treated with other urinary diversion methods ($n=19$). The IONB was constructed using the Studer technique; the surgical procedure was described previously.^[13] Ultimately, 287 patients with a Studer IONB after RC were analyzed.

The patients were divided into 2 groups according to the pattern of use of prophylactic antibiotics. During the period from January 2012 through November 2015, prophylactic antibiotics were used in 3 stages (long-term group). On the day of surgery, a third-generation cephalosporin (3GC), aminoglycoside, and metronidazole were administered intravenously, followed by about 10 days of intravenous (IV) 3GC. Then, an oral 3GC, fluoroquinolone, or trimethoprim/sulfamethoxazole was used for 2 weeks. However, after December 2015, cefotetan was administered on the day of surgery, just before start of surgery, and after 12 and 24 hours of initial cefotetan administration (short-term group). We used a 1-month (December 2015) wash-out period before switching the prophylactic antibiotic use. Urine culture was performed when the patient was febrile in both groups. In the short-term group, routine urine culture was performed before removing the urinary catheter, usually 7 to 10 days after surgery.

2.2. Definitions

Bacteriuria was defined as a positive urine culture after IONB surgery following RC with or without symptoms. Febrile urinary tract infection (FU) was defined as bacteriuria with a body temperature over 38°C, without any other obvious infectious foci. Bacteremia was defined as positive blood cultures after RC with an IONB. We considered FU and bacteremia as infectious complications, which were assessed during the 90-day period after surgery.

The development of *Clostridium difficile*-associated diarrhea (CDAD) was assessed to evaluate adverse reactions to antibiotic use. The definition of CDAD was a positive result for any of the following: *C difficile* culture, toxin polymerase chain reaction, or toxin enzyme immunoassay. CDAD was also assessed during the 90 days after RC with an IONB.

Antibiotic-resistant organisms were defined as follows: vancomycin-resistant enterococci (VRE), methicillin-resistant staphylococci, 3GC-resistant streptococci as antibiotic-resistant Gram-positive bacteria, 3GC-resistant Enterobacteriaceae, and carbapenem-resistant non-fermenters as antibiotic-resistant Gram-negative bacteria.

2.3. Outcome measures

The primary outcome of the study was the proportion of FU within 60 days of RC with an IONB in both groups. The secondary outcomes were as follows: proportion of bacteriuria, FU within 30 or 90 days of RC with an IONB, FU during the same admission as surgery, bacteremia within 90 days of RC with an IONB, urinary colonization with antibiotic-resistant organisms, and the development of CDAD.

2.4. Statistical analysis

Continuous variables are presented as means (standard deviation [SD]) and categorical variables are presented as absolute values (percentage). Descriptive statistics were obtained for demographic variables. The independent *t* test was used to compare continuous variables and Pearson's chi-square test was used to

compare baseline characteristics and the incidence of infectious complications. A Kaplan–Meier survival analysis was used to examine bacteriuria, FU, and bacteremia, and the log-rank test was applied to compare outcomes between the 2 groups. Multivariate logistic regression analyses were performed using variables that may affect the development of postoperative (post-Op) complications. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY). A 2-sided *P* value <.05 was taken to indicate statistical significance. This study was approved by the Institutional Review board of Ewha Womans University Mokdong Hospital.

3. Results

3.1. Baseline characteristics

The baseline demographics and clinical characteristics of 287 patients undergoing RC with an IONB for bladder cancer are summarized in Table 1. The baseline characteristics were similar for 2 groups of patients divided according to the use of prophylactic antibiotics (long-term vs short-term group), but the length of stay was significantly shorter in the short-term group compared to the long-term group (24.4 vs 18.6 days, respectively, $P<.001$) (Table 1). None of the enrolled patients underwent neoadjuvant chemotherapy and therapeutic antibiotic use before surgery.

3.2. Comparison of infectious complications

Infectious complications after RC with an IONB are summarized in Table 2. Bacteriuria occurred more frequently in the long-term group than the short-term group (49.2% vs 84.3%, respectively, $P<.001$). The development of bacteriuria occurred significantly earlier in the long-term group ($P<.001$, Fig. 1). However, the proportion of patients with FU was not different between the 2 groups at any time point. The rates of FU within 60 days of surgery were 28.6% in the short-term group and 28.4% in the long-term group ($P=.969$). The interval of FU development after surgery was also not significantly different between the 2 groups ($P=.843$, Fig. 2). The proportion of patients with bacteremia was also not significantly different between the short-term group and the long-term group (5.4% vs 7.8%, $P=.415$, Fig. 3). The rate of CDAD development was not different between the 2 groups (5.4% vs 6.9%, $P=.617$). The rate of surgical site infection was slightly higher in the long-term group than the short-term group (4.3% vs 11.8%, $P=.018$). However, 4 cases of surgical site infection in the long-term group were related to mechanical complications at the IONB or small bowel anastomosis site. In multivariate analyses, female gender was associated with development of FU, but administration of short-term prophylactic antibiotics was not (Table 3).

3.3. Microorganisms in infectious complications

Urine was colonized more frequently with Gram-positive bacteria than Gram-negative bacteria in the initial 90 days after RC with an IONB (Table 4A). In the short-term group, *Enterococcus faecium* was the most frequently isolated organism ($n=41$, 45.1%), and was detected more frequently than in the long-term group (45.1% vs 10.5%, $P<.001$). The rate of VRE (both of *Enterococcus faecalis* and *E. faecium*) was also higher in the short-term group (13.2% vs 2.3%, $P=.007$). Viridans streptococci were isolated in the long-term group, but none were

Table 1**Baseline characteristics between pre-intervention and post-intervention groups.**

Characteristics	Long-term group N = 185	Short-term group N = 102	P value
Sex (male)	159 (85.9%)	91 (89.2%)	.43
Age (years, mean (\pm SD))	62.6 (\pm 10.4)	62.9 (\pm 10.5)	.74
Body mass index (kg/m ² , mean (\pm SD))	24.4 (\pm 2.9)	24.2 (\pm 3.3)	.68
Diabetes mellitus, well controlled (HbA1C under 8%)	24 (13.0%)	17 (16.7%)	.43
Diabetes mellitus, poorly controlled (HbA1C over 8%)	8 (4.3%)	2 (2.0%)	
Length of stay (days, mean (\pm SD))	24.4 (10.3)	18.6 (7.2)	<.01
Length of stay in cases with FU during the admission	32.5 (12.9)	21.5 (7.7)	<.01
Length of stay in cases without FU during the admission	23.0 (9.1)	17.6 (7.0)	<.01
PreOp length of stay (days, mean (\pm SD))	3.8 (2.0)	2.9 (1.1)	<.01
preOp length of stay in cases with FU during the admission	4.1 (3.2)	3.1 (1.3)	.12
preOp length of stay in cases without FU during the admission	3.8 (2.0)	2.9 (1.1)	<.01
PostOp length of stay (days, mean (\pm SD))	20.5 (9.8)	18.5 (7.0)	<.01
PostOp length of stay in cases with FU during the admission	28.4 (12.4)	18.4 (7.4)	<.01
PostOp length of stay in cases without FU during the admission	19.3 (8.5)	14.7 (6.9)	<.01
Operation time (min, mean (\pm SD))	313.5 (\pm 57.2)	293.7 (\pm 47.2)	<.01
Estimated blood loss (mL, mean (\pm SD))	728.2 (\pm 445.8)	532.9 (\pm 300.7)	<.01

FU = febrile urinary tract infection, postOp = postoperative, preOp = preoperative, SD = standard deviation.

detected in the short-term group (0% vs 33.7%, $P < .001$). Enterobacteriaceae resistant to 3GC (*Escherichia coli* or *Klebsiella pneumoniae*) that produced extended spectrum beta-lactamase (ESBL) or other 3GC resistant Enterobacteriaceae were also detected at a higher rate in the short-term group (40.7% vs. 14.0%, $P < .001$) (Table 4A).

Among the 85 cases of FU within 90 days of surgery, 54 and 31 were in the short-term group and the long-term group, respectively (Table 4B). *Enterococcus faecium* was the most frequently isolated microorganism in the short-term group ($n = 22$, 40.7%), and 4 (7.4%) of the isolates were VRE. In the long-term group, *Enterococcus faecalis* was the most frequently isolated microorganism ($n = 8$, 25.8%), and all of the *E faecalis* isolates were susceptible to ampicillin. Enterobacteriaceae that were resistant to 3GC were also present at higher rates in the short-term group than the long-term group (33.3% vs 6.5%, respectively, $P = .005$). There were 8 cases of viridans streptococci-related FU in the long-term group, among which 3 were 3GC-resistant isolates, whereas no cases of viridans streptococci-related FU were seen in the short-term group. In both groups, enterococci were frequent causes of bacteremia (50% vs 25.0%, respectively) (Table 4C). Carbapenem-resistant Enterobacteriaceae were not isolated in either group.

4. Discussion

We assessed the pattern of prophylactic antibiotics, from 4 weeks of multiple antibiotics to 24 hours of a single agent and found that these changes did not increase the rates of major infectious complications, including FU and bacteremia, although the rate of bacteriuria was higher in the short-term prophylaxis group. As an IONB is reconstructed from the ileum, surgical prophylaxis in RC with an IONB is guided according to recommendations for intestinal surgery. Current major guidelines recommend the use of a first-generation cephalosporin with metronidazole or second-generation cephalosporin (2GC) in urological surgery manipulating the intestine.^[12,14] They also recommend less than 24 hours of prophylactic antibiotic use. Although the major bacterial organisms were Enterococcus in our study, we accepted this recommendation as our policy because of the following reasons. First, Enterococcus were known to have lower virulence than other Gram-positive cocci, such as *Staphylococcus aureus*, or other enteric Gram-negative bacteria. Second, because the objective of surgical prophylactic antibiotics is to prevent infections resulting from skin bacterial flora after skin incision, activity against *Staphylococcus* is more important than that against Enterococcus. Third, to protect against Enterococcus, we should use ampicillin-sulbactam or piperacillin-tazobactam as

Table 2**Infectious complications after radical cystectomy with an ileal orthotopic neobladder surgery in pre-intervention and post-intervention groups.**

Infectious complications	Long-term group N = 185	Short-term group N = 102	P value
Bacteriuria within 7-days of surgery	11 (5.9%)	52 (51.0%)	<.01
Bacteriuria within 14-days of surgery	45 (24.3%)	77 (75.5%)	<.01
Bacteriuria within 30-days of surgery	71 (38.4%)	79 (77.5%)	<.01
Bacteriuria within 60-days of surgery	84 (45.4%)	83 (81.4%)	<.01
Bacteriuria within 90-days of surgery	91 (49.2%)	86 (84.3%)	<.01
FU during the same admission of surgery	34 (18.4%)	24 (23.5%)	.37
FU within 30-day of surgery	46 (24.9%)	24 (23.5%)	.80
FU within 60-day of surgery	53 (28.6%)	29 (28.4%)	.97
FU within 90-day of surgery	54 (29.2%)	31 (30.4%)	.83
Bacteremia	10 (5.4%)	8 (7.8%)	.42
CDAD	10 (5.4%)	7 (6.9%)	.62
Surgical site infection	8 (4.3%)	12 (11.8%)	.02

CDAD = *Clostridium difficile*-associated diarrhea, FU = febrile urinary tract infection.

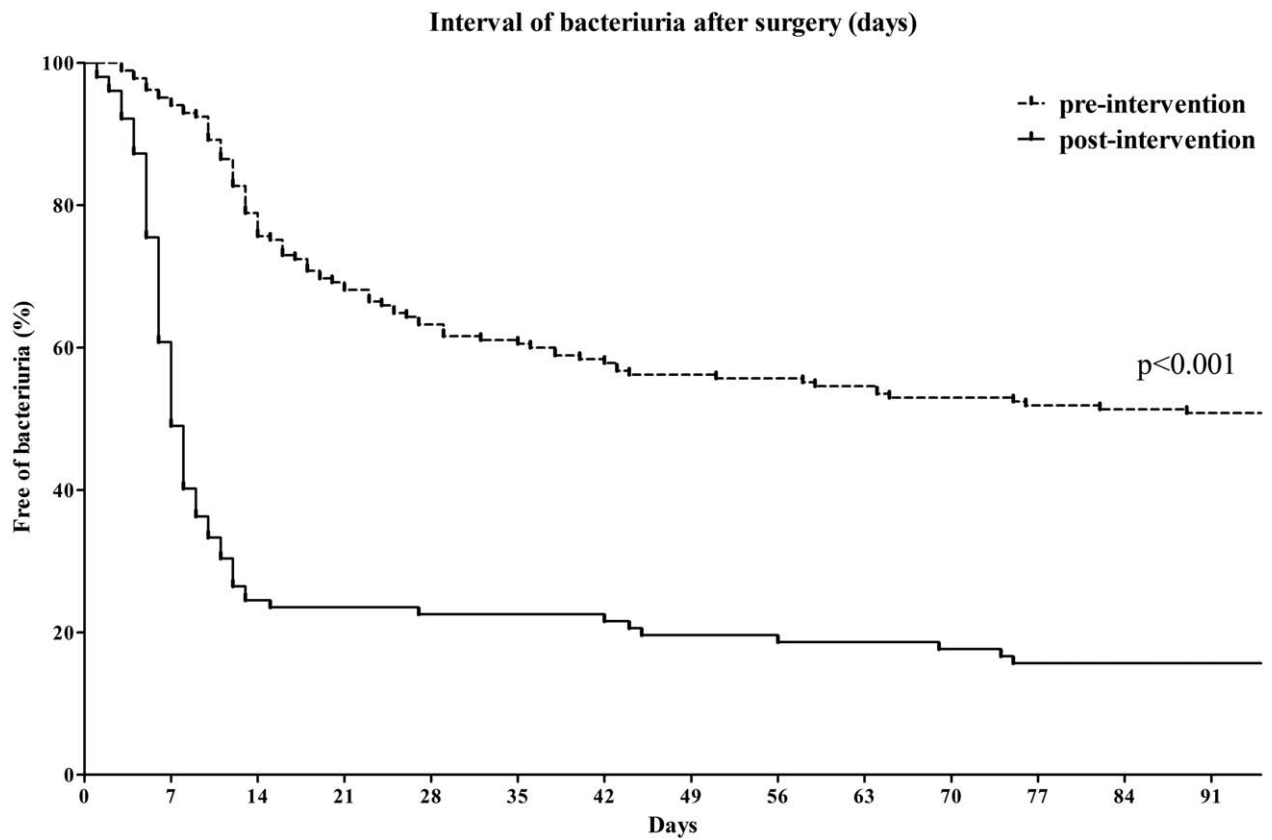


Figure 1. Comparison of the time to bacteriuria development after radical cystectomy and neobladder surgery.

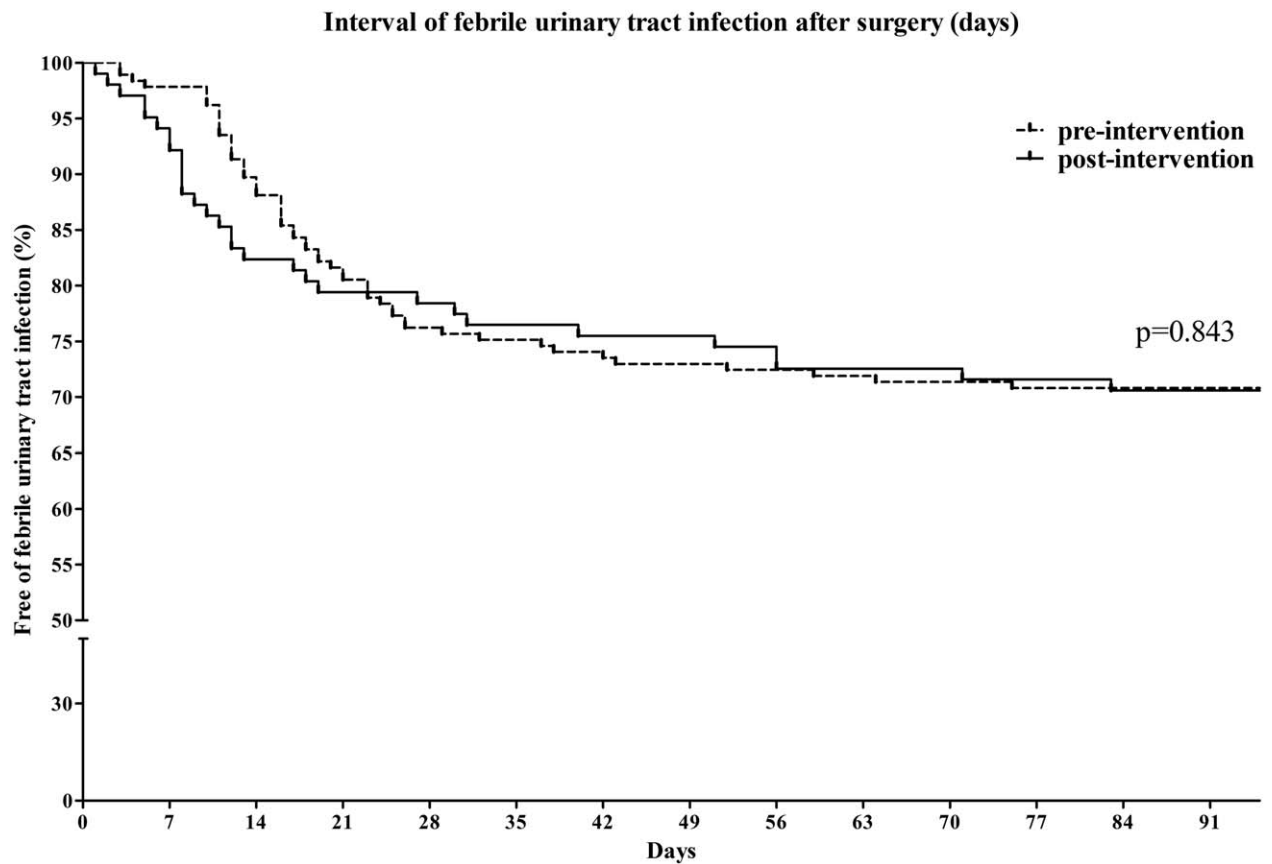


Figure 2. Comparison of the time to occurrence of a febrile urinary tract infection after radical cystectomy and neobladder surgery.

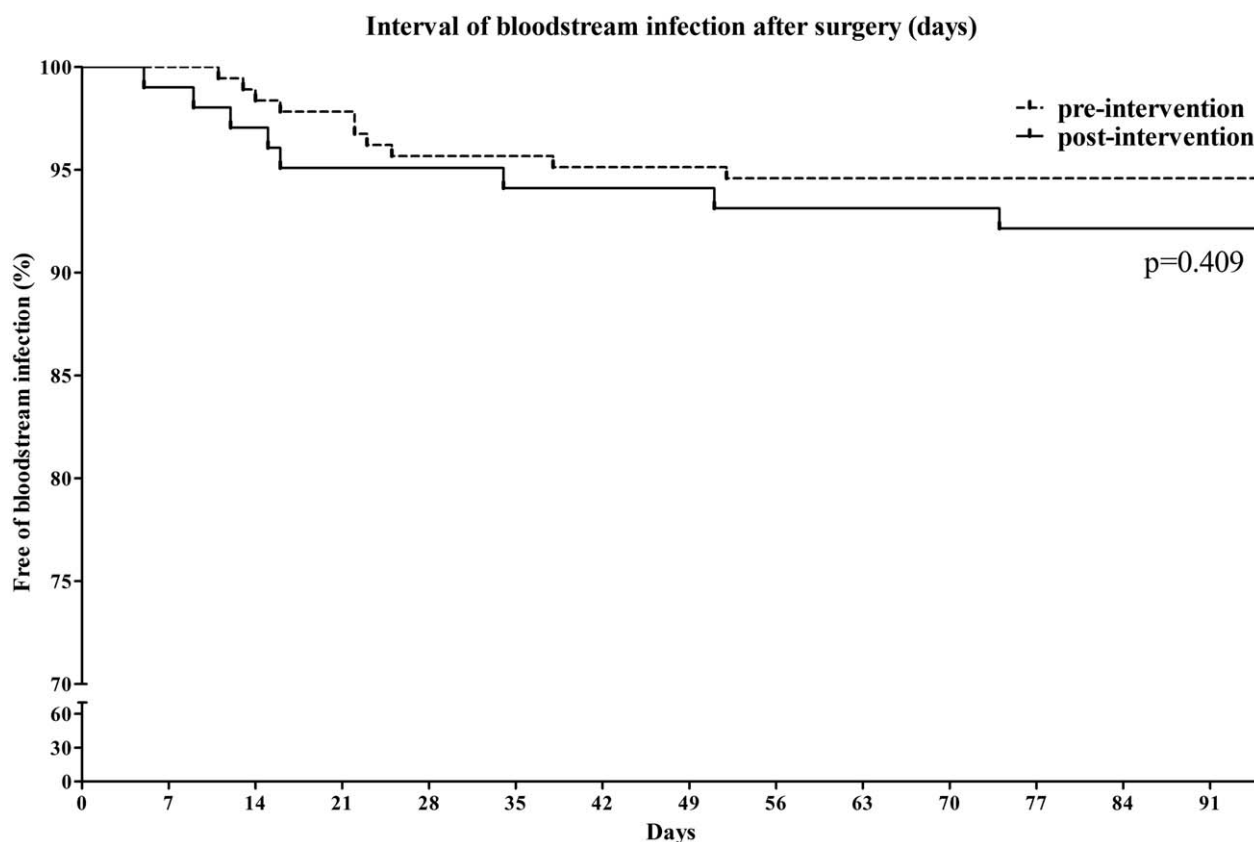


Figure 3. Comparison of the time to occurrence of bacteremia after radical cystectomy and neobladder surgery.

prophylactic antibiotics, which have broader antibiotic spectrum than current recommendation, and this would result in a negative effect on antibiotic stewardship. These guidelines are highly supported by recent studies indicating no increase in surgical site infection rates associated with short-term antibiotic prophylaxis in colorectal surgery.^[15,16] In urological surgery, there have been reports of short-term antibiotic prophylaxis,^[17] but such reports in RC are scarce. Recently, large-scale data regarding the association between prophylactic antibiotics and infectious complications in RC were reported in the USA. In this study, short-term antibiotic use was not associated with increased

infectious complications.^[18] However, there were relatively few cases of continent diversion, which showed higher rates of infectious complications. Our data show that the rate of FU was not different between the short-term group and long-term group. Therefore, we suggest that short-term antibiotic prophylaxis is effective in RC with an IONB, in accordance with previous reports.

In studies of the long-term outcomes of RC, urinary tract infection mostly occurred within the first 3 months after surgery.^[19,20] Therefore, infectious complications in the initial 3 months remain the major concern in RC with an IONB. In the

Table 3

Multivariate analyses of factors associated with occurrence of febrile urinary tract infection.

Variables	Febrile urinary tract infection (n=85)	No febrile urinary tract infection (n=202)	P value	Adjusted odds ratio (95% CI)	P value
Age (years, mean (±S.D))	62.7 (±11.1)	62.7 (±10.1)	.99	0.99 (0.97–1.02)	.87
Sex					
male	66 (77.6%)	184 (91.1%)	<.01	1.00	<.01
female	19 (22.4%)	18 (8.9%)		3.05 (1.49–6.23)	
Body mass index (kg/m ² , mean (±S.D))	24.4 (±3.6)	24.3 (±2.9)	.90	0.99 (0.91–1.08)	.88
Operation time (min, mean (±S.D))	312.1 (±50.5)	304.0 (±56.2)	.23	1.00 (0.99–1.01)	.13
Estimated blood loss (mL, mean (±S.D))	646.4 (±312.1)	664.0 (±446.1)	.70	1.00 (0.99–1.00)	.47
Diabetes mellitus	18 (21.2%)	33 (16.3%)	.33	1.52 (0.78–2.94)	.22
PreOp length of stay (days, mean (±S.D))	3.6 (±2.3)	3.5 (±1.8)	.61	1.05 (0.92–1.19)	.49
Pattern of prophylactic antibiotics					
Short-term group	31 (36.5%)	71 (35.1%)	.83	1.00	.56
Long-term group	54 (63.5%)	131 (64.9%)		0.84 (0.48–1.50)	

CI = confidence interval, preOp = preoperative, SD = standard deviation.

Table 4

Microorganisms in infectious complications.

(A) Microorganisms in bacteriuria			
Microorganisms	Long-term group N=91	Short-term group N=86	P value
Gram positive bacteria colonization	67 (73.6%)	76 (88.4%)	.01
<i>Enterococcus faecalis</i>	26 (28.6%)	33 (38.4%)	.17
Ampicillin susceptible	22 (24.2%)	32 (37.2%)	.06
Ampicillin resistant, vancomycin susceptible	5 (5.5%)	1	.21 [†]
vancomycin resistant	0	1	.49 [†]
<i>Enterococcus faecium</i>	41 (45.1%)	9 (10.5%)	<.01
Ampicillin susceptible	2 (2.2%)	1	1.00 [†]
Ampicillin resistant, vancomycin susceptible	28 (30.8%)	7 (8.1%)	<.01
vancomycin resistant	12 (13.2%)	1	<.01
Viridans streptococcus	0	29 (33.7%)	<.01
3GC resistant	0	11 (12.8%)	<.01
Staphylococcus species	1	11 (12.8%)	<.01
Methicillin susceptible <i>S. aureus</i>	0	0	
Methicillin resistant <i>S. aureus</i>	1	1	
Methicillin susceptible Coagulase negative Staphylococci	0	2	
Methicillin resistant Coagulase negative Staphylococci	0	8 (9.3%)	
Gram negative bacteria colonization	46 (50.5%)	45 (52.3%)	.81
<i>Escherichia coli</i>	24 (26.4%)	11 (12.8%)	.02
ESBL-producing <i>E. coli</i>	20 (22.0%)	5 (5.8%)	<.01
Klebsiella species	11 (12.1%)	7 (8.1%)	.39
ESBL-producing Klebsiella species	11 (12.1%)	2	.01
Other Enterobacteriaceae	8 (8.8%)	9 (10.5%)	.71
3GC resistant	6 (6.6%)	5 (5.8%)	.83
<i>Acinetobacter baumannii</i>	1	13 (15.1%)	<.01
Carbapenem resistant <i>A. baumannii</i>	1	1	1.00 [†]
Other <i>Acinetobacter</i> species	1	9 (10.5%)	<.01 [†]
<i>Pseudomonas</i> species	1	2	.61
<i>Proteus</i> species	2 (2.2%)	0	.50
Others	1	5 (5.8%)	.11 [†]
<i>Candida</i> species	7 (7.7%)	4 (4.7%)	.40

(B) Microorganisms in febrile urinary tract infections

Microorganisms	Long-term group N=54	Short-term group N=31	P value
<i>Enterococcus faecalis</i>	11 (20.4%)	8 (25.8%)	.56
Ampicillin susceptible	10 (18.5%)	8 (25.8%)	.43
Ampicillin resistant, vancomycin susceptible	1	0	1.00 [*]
<i>Enterococcus faecium</i>	22 (40.7%)	4 (12.9%)	<.01
Ampicillin susceptible	1 (1.9%)	0	1.00 [*]
Ampicillin resistant, vancomycin susceptible	17 (31.5%)	4 (12.9%)	.06
vancomycin resistant	4 (7.4%)	0	.29 [*]
Viridans streptococcus	0	8 (25.8%)	<.01
3GC resistant	0	3 (9.7%)	.05 [*]
<i>E. coli</i>	11 (20.4%)	2 (6.5%)	.12 [*]
ESBL-producing <i>E. coli</i>	11 (20.4%)	1 (3.2%)	.05 [*]
Klebsiella sp	4 (7.4%)	2 (6.5%)	1.00 [*]
ESBL-producing Klebsiella species	4 (7.4%)	1 (3.2%)	.65 [*]
Other Enterobacteriaceae	3 (5.6%)	1 (3.2%)	1.00 [*]
3GC resistant	3 (5.6%)	0	.30 [*]
<i>Acinetobacter baumannii</i>	1	3 (9.7%)	.14 [*]
Carbapenem resistant <i>A. Baumannii</i>	1	0	1.00 [*]
<i>Candida albicans</i>	2	0	.53 [*]
Other gram positive cocci	0	2	.13

(C) Microorganisms in bacteremia

Microorganisms	Long-term group n=10	Short-term group n=8
<i>E. faecalis</i> (ampicillin susceptible)	2	0
<i>E. faecium</i>	3	2
Ampicillin resistant, vancomycin susceptible	2	1
Vancomycin resistant	1	1
<i>Enterococcus hirae</i>	0	1
<i>E. coli</i> (ESBL-producing)	3	1
<i>Klebsiella pneumoniae</i> (ESBL-producing)	1	1
<i>Burkholderia cepacia</i>	1	0
<i>Bacteroides fragilis</i>	0	1
Coagulase negative staphylococcus species	0	2

* multiple organisms were isolated in some cases.

[†] fisher exact test.^{*} fisher exact test.

3GC=Third generation cephalosporin, ESBL=extended spectrum beta-lactamase.

present study, we found that the incidence of FU after RC with an IONB in the first 90 days after surgery was 29%. Previous studies have reported incidence rates of FU after continent urinary diversion in RC ranging from 15% to 43%.^[6,8,10,20] The variabilities in the incidence of UTI were probably due to the definition of UTI and methods of urinary diversion. Ross et al reported a lower rate of UTI, defined by the use of ICD-9 codes, that included pyelonephritis and cystitis.^[18] However, the number of cases of continent diversion in that study accounted for only 5.2% of the total study population. Shigemura et al reported that UTI accounted for 38.6% of infectious complications after RC with an IONB, which is comparable to our results.^[11]

Although the occurrence of bacteriuria was significantly higher in the long-term group, the rates of UTI development were similar in both groups. Such differences in colonization and infection were also reported in previous studies,^[10,20,21] suggesting that bacterial colonization of an IONB does not proceed to a UTI in most cases. The duration of prophylactic antibiotic use was also unrelated to the rate of UTIs, and the proportion of UTIs in both groups converged within 3 months. The reason for the lack of UTI development despite the high rate of bacteriuria is unclear, but some factors may play preventive roles in an IONB. The ileal mucosa has innate tolerance to colonization by various types of bacteria because it is continuously exposed to bowel contents,^[22] thus, an IONB favors the asymptomatic carriage of bacteria.^[21] In addition, the adaptation of the mucosa of an IONB to urine flow after surgery may lead to fewer UTIs. Kojima et al reported that marked mucosal changes occurred in the ileal mucosa after IONB surgery.^[23]

In the present study, the urinary microbial colonization pattern and microbiological causes of FU were markedly different between the short-term group and the long-term group. As there have been no previous studies comparing urinary colonization patterns associated with changes in prophylactic antibiotic use, we were unable to compare our results with those of previous studies. In the present study, we did find some altered patterns after changes in prophylactic antibiotics. First, there was an increase in the proportion of *E faecalis*, which is known to show reduced virulence and resistance. Second, multi-drug-resistant organisms such as VRE or 3GC-resistant Enterobacteriaceae were decreased, probably due to less antibiotic pressure.

In this study, we changed the prophylactic antibiotics from a 3GC to a 2GC. Due to the anti-anaerobic effect of 2GCs, there were concerns regarding the potential risk of a *C difficile* infection.^[24,25] The development of severe fulminant CDAD after short-term use of prophylactic cefuroxime in orthopedic patients was reported previously.^[26] However, previous studies have suggested mixed results after CDAD and 2GC antimicrobial prophylaxis.^[24,25,27] In the present study, the CDAD rate was similar between the short-term period and long-term period. Although changing the prophylactic antibiotics to a 2GC did not affect the incidence of CDAD, our result (4.9% of RC with IONB patients) is relatively high compared to those reported in other countries. In the USA, the reported general incidence rate of CDAD after surgery is 0.5% and 0.9% in patients with bowel resection or repair.^[28] The reported incidence of CDAD after radical cystectomy was 1.0% to 7.0%.^[7,9,29-31] Although RC is a risk factor for CDAD in various urological surgeries,^[32] our results show a relatively high incidence of CDAD. However, some investigations examined the trends toward higher incidence rates of *C difficile* infection in studies with medical record review

^[30,31] than in studies using claim data or nationwide sample data,^[9,29] which have a probable reporting bias. Our results regarding the incidence of *C difficile* infection were comparable to those of previous studies that directly reviewed the medical records of patients with RC.

This study had some limitations. First, because more attention was given to infectious complications after short-term use of prophylactic antibiotics, more frequent urinary cultures were obtained in the long-term group. This may have contributed to an increase in the documented incidence of bacteriuria in the long-term group. Second, the preoperative (preOp) length of stay was shorter in the long-term group for 1 day, because preOp risk evaluation was performed at an outpatient clinic in this period. Although a longer length of stay is a risk factor for acquisition of resistant organisms, the differences in time were short, and it might not affect the colonization rate of resistant organisms. Third, because of its retrospective design, some cases of surgical site infection could have been missed in the earlier parts of the study period. Fourth, although, we found that the short-term use of prophylactic antibiotics is effective, the results should be confirmed by a prospective controlled study using various regimens of prophylactic antibiotics to provide solid evidence.

In conclusion, this study suggests that short-term prophylactic use of a 2GC rather than long-term antibiotic prophylaxis is effective in preventing FU in RC with an IONB and in decreasing colonization with multi-drug-resistant organisms.

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