Comparison of Different Rectal Cleansing Methods for Reducing Post-Procedural Infectious Complications After Transrectal Ultrasound-Guided Prostate Biopsy

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Purpose: To compare the efficacy of three different rectal cleansing methods for reducing post-procedural infectious complications after transrectal ultrasound (TRUS)-guided prostate biopsy.

Materials and Methods: A total of 451 consecutive patients who underwent TRUS-guided prostate biopsy were prospectively included in this study. All patients received targeted antimicrobial prophylaxis and underwent bowel preparation through laxative administration. The patients were divided into three groups on the basis of the method of rectal cleansing immediately before the procedure. Group I patients (n =165) underwent cleansing of the perianal skin using povidone-iodine cotton balls; group II patients (n=116) received an injection of povidone-iodine solution (0.1 g/mL) into the anal and lower rectal canals; and group III patients (n =170) received direct manual cleansing of the mucosal surface of the anus and lower rectum using povidone-iodine cotton balls. The three groups were compared regarding the incidence of post-procedural infectious complications, re-hospitalization rates, and mean length of hospital stay using one-way ANOVA, the Chi-square test, and multiple logistic regression analysis.

Results: Post-procedural infectious complications occurred in %11.2 ,%21.8, and %6.5 of groups I, II, and III, respectively (P < .001). The incidence of overall infectious complications was significantly lower in group II (%95 CI: 0.958–0.232, OR = 0.472, P = .038) and group III (%95 CI: 0.555–0.129, OR = 0.267, *P* < .001) than in group I. Re-hospitalization rates were %2.6 ,%9.7, and %0.6 in groups I, II, and III, respectively (*P* < .001). The incidence of re-hospitalization was significantly lower in group II (%95 CI: 0.869–0.070, OR = 0.247, *P* = .029) and group III (%95 CI: 0.421–0.007, OR = 0.055, *P* = .005) than in group I. The mean length of hospital stay was significantly longer in group I than in group III (*P* = .009).

Conclusion: Combined with targeted antimicrobial prophylaxis, direct manual cleansing of the mucosal surface of the anus and lower rectum using povidone-iodine cotton balls was most effective in preventing post-procedural infectious complications among the three different rectal cleansing methods.

Keywords: biopsy; infection; prostate; sepsis; transrectal

INTRODUCTION

Transrectal ultrasound (TRUS)-guided prostate biopsy in patients with suspected prostate cancer is currently the gold-standard procedure for prostate cancer diagnosis.[1] Although it is generally recognized as safe and well tolerated, TRUS-guided prostate biopsy is an invasive method of obtaining prostate tissue samples that may occasionally cause serious complications. Whereas the reported overall complication rates after prostate biopsy vary widely in previous studies, ranging from 2% to 10.4%, the rates of infectious complication requiring hospitalization range from 0% to 6.3%.[2-4] Indeed, infectious complications are a leading cause of prolonged hospital stay and financial burden after prostate biopsy. Therefore, numerous strategies have been proposed to minimize those complications.[5-7]

As it was shown to be effective in reducing the rate of infectious complications before colorectal surgery,[8] rectal cleansing before prostate biopsy, along with prophylactic antibiotics, is well known to reduce the risk of infectious complications.[9] A recent systemic review and meta-analysis revealed that rectal cleansing using povidone-iodine before prostate biopsy significantly reduced the rate of infectious complications compared to the control group.[10] When a combination of povidone-iodine and prophylactic antibiotics is used, these effects are further accentuated.[4,10] However, as optimal rectal cleansing methods have not been standardized, various protocols have been used.[11-13] Raman et al. reported that soaking the rectum and painting the perianal area with povidone-iodine gauze before prostate biopsy reduced the post-biopsy infectious complications rate from 4.3% to 0.6%.[12] In a study by AbuGhosh et al., the anterior rectal mucosa was directly cleansed using an examiner's finger and a thin layer of gauze soaked in

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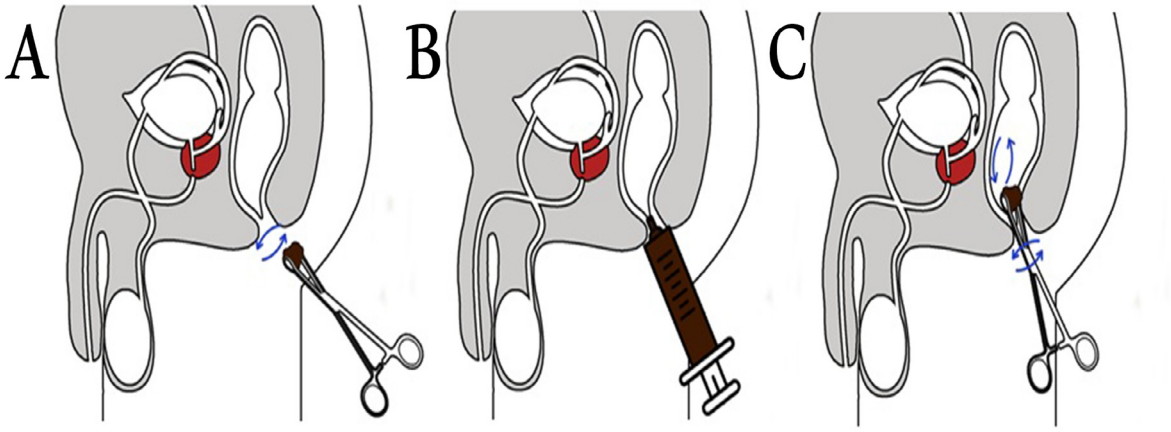

Figure 1. Illustrations showing the three different rectal cleansing methods.
A. Group I: cleansing of the perianal skin using povidone-iodine cotton balls. **B.** Group II: injection of povidone-iodine solution (0.1 g/mL) into the anal and lower rectal canals. **C.** Group III: direct manual cleansing of the mucosal surface of the anus and lower rectum using povidone-iodine cotton balls.

povidone-iodine.[13] To the best of our knowledge, the effectiveness of these various methods of rectal cleansing has not been meticulously compared.
Therefore, the aim of this study was to compare the efficacy of different rectal cleansing measures for reducing post-procedural infectious complications after TRUS-guided prostate biopsy.

MATERIALS AND METHODS

Patients

This study was approved by our institutional review board, and written informed consent was obtained from all patients. During a one-year of study period, 456 consecutive patients from a single tertiary center who underwent TRUS-guided prostate biopsy under hospitalization were prospectively included in this study. Among them, five patients who did not undergo rectal swab culture for the targeted antimicrobial prophylaxis because of the following reasons were excluded from the study: (1) four patients were already hospitalized for the evaluation of bone metastasis of unknown origin, and (2) one patient was already on antibiotic treatment because of a severe urinary tract infection (UTI). Finally, 451 patients were enrolled in this study.
The indications for biopsy were as follows: (1) prostate specific antigen (PSA) value greater than 4 ng/mL (n = 407, 90.2%); (2) concerning findings on digital rectal examination such as a nodule, induration, and asymmetry or concerning abnormal lesions on TRUS or prostate MR imaging (n = 16, 3.5%); (3) the presence of both (1) and (2) (n = 24, 5.3%); and (4) atypia on a previous prostate needle biopsy (n = 4, 0.9%). During the study period, one of three different rectal cleansing methods was used just prior to the procedure. The rectal cleansing method was applied differently every month for randomization. Each method was used for a total of four months during the study period of one year. Group I patients underwent cleansing of the perianal skin using povidone-iodine cotton balls (**Figure 1A**); group II patients received an injection of povidone-iodine solution (0.1 g/mL) into the anal and lower rectal canals (**Figure 1B**); group III patients underwent direct manual cleansing of the mucosal surface of the anus and lower rectum using forceps and povidone-iodine cotton balls (**Figure 1C**).

Pre-procedural Preparations

All patients were admitted to the hospital one day prior to the procedure. They received targeted antimicrobial prophylaxis on the basis of the rectal swab culture results. The rectal swab samples were obtained two weeks before the biopsy and cultured on MacConkey's agar (KOMED) containing 1 μg/mL ciprofloxacin overnight at 37°C in ambient air. All isolates were subjected to organism identification and antimicrobial susceptibility testing using an automated microbial system (VITEK® 2). If quinolone resistance was not observed in the results of the rectal swab culture, the patients received antibiotic prophylaxis consisting of a total of three intravenous injections of ciprofloxacin (400 mg) at morning and evening of day of biopsy, and the morning after the procedure. However, in cases of quinolone resistance, the patients received a total of three intravenous injections of prophylactic ceftriaxone (500 mg) before and after the procedure. All patients also underwent bowel preparation using laxatives the day before the procedure. To minimize pain during the procedure, intravenous dripping of 100 mL of physiologic saline mixed with ketamine (10 mg/mL) was started one hour prior to the biopsy.

Biopsy Protocol

The patient was positioned in the left lateral decubitus position with their knees bent. All patients underwent rectal cleansing using one of three different methods immediately before the procedure. TRUS-guided prostate biopsy was performed using an 18-gauge fully automated biopsy gun with a needle length of 20 cm, cutting notch size of 1.6 cm, and stroke length of 22 mm (Acecut; CIVCO Medical Solutions, Kalona, IA, USA) under ultrasonographic guidance (LOGIC E9; GE Healthcare, Milwaukee, WI, USA) by one experienced radiologist. During the procedure, the biopsy needle was inserted via a steering device attached to the 5.0 to 7.5 MHz transducer to visualize the needle path parallel to the electronic guideline provided by the US images. A total of eight tissue specimens were taken from the prostate gland, with two cores in each of the

Table 1. Demographics and clinical characteristics of patients.

	Group I (N = 165)	Group II (N = 116)	Group III (N = 170)	*P*-value
Age, year; mean ± SD	68.63 ± 8.11	68.94 ± 8.52	67.49 ± 8.54	.282
Prostate volume, cc; mean ± SD	45.48 ± 27	41.57 ± 22.51	36.72 ± 15.59	.001
PSA level, ng/mL; median (IQR)	6.4 (3.6-10.5)	6.0 (4.2-10.1)	6.7 (4.3-11.9)	.083
Diabetes mellitus (%)	30 (18.2)	23 (19.8)	33 (19.4)	.932
Chronic kidney disease (%)	12 (7.3)	15 (12.9)	29 (17.1)	.025
Foley catheter insertion state (%)	6 (3.6)	2 (1.7)	3 (1.8)	.457
Recent antimicrobial use (%)	27 (16.4)	24 (20.7)	24 (14.1)	.339
Recent hospitalization (%)	16 (9.7)	9 (7.8)	10 (5.9)	.427
Recent history of UTI or prostatitis (%)	10 (6.1)	9 (7.8)	13 (7.6)	.809
Recent history of prostate biopsy (%)	1 (0.6)	1 (0.9)	3 (1.8)	.574
FQ resistance (%)[a]	55 (33.3)	53 (45.7)	89 (52.4)	.002
Rectal swap culture result				.102
E. coli (%)	147 (89.1)	106 (91.4)	144 (84.7)	
K. pneumonia (%)	2 (1.2)	5 (4.3)	8 (4.7)	
Other (%)	9 (5.5)	5 (4.3)	8 (4.7)	
No growth (%)	7 (4.2)	0 (0)	10 (5.9)	
Biopsy result				.140
BPH (%)	99 (60)	55 (47.4)	83 (48.8)	
Prostate cancer (%)	59 (35.8)	52 (44.8)	81 (47.6)	
ASAP (%)	4 (2.4)	7 (6.0)	5 (2.9)	
Other (%)	3 (1.8)	2 (1.7)	1 (0.6)	

Abbreviations: PSA, Prostate Specific Antigen; IQR, Interquartile Range; UTI, Urinary Tract Infection; FQ, Fluoroquinolone; BPH, Benign Prostate Hyperplasia; ASAP, Atypical Small Acinar Proliferation.
aOverall FQ resistance was 43.7%.

four regions (right upper, right lower, left upper, and left lower) of the prostate gland. Further, in cases with a suspicious focal lesion in the middle part in both prostate glands on ultrasound images, tissue samples were additionally obtained at those portions. Immediately after the core tissues were extracted, manual compression of the prostate gland using the US probe was performed to prevent possible post-procedural bleeding. In addition, color Doppler US was performed to carefully check for any significant post-biopsy bleeding. The patients were discharged the day after the procedure if there were no complications, and they were routinely followed up on an out-patient basis within one month after discharge. In cases of unexpected complications, they were re-admitted via the emergency department.

Data Analysis

The electronic medical records of three groups were meticulously analyzed, including demographic data, prostate volume, PSA level, presence of infectious and non-infectious complications, and underlying disease including diabetes mellitus (DM), by one urologist who was blinded to the information regarding the rectal cleansing method applied to the patients. Moreover, past history of Foley catheter insertion within one month before the procedure, antimicrobial use within three months, UTI or prostatitis within three months, hospitalization within six months, prostate biopsy within one year, and fluoroquinolone (FQ) resistance were also investigated. The presence or absence of FQ resistance was determined by the culture results of the rectal swab samples obtained two weeks before the biopsy. Infectious complications after biopsy were considered present if the patients showed asymptomatic bacteriuria or pyuria, symptomatic UTI or prostatitis with or without fever (> 37.8 °C), bacteremia, sepsis, or systemic inflammatory response syndrome (SIRS) at any time up to one month after the procedure. SIRS was defined by the presence of two of the following clinical findings: body temperature higher than 38 °C or lower than 36 °C, heart rate higher than 90/min, hyperventilation evidenced by a respiratory rate higher than 20/min or PaCO2 lower than 32 mmHg, and white blood cell count higher than 12,000/μL or lower than 4,000/μL.[14] Re-hospitalization was defined as re-admission to the hospital due to infectious complications related to the TRUS-guided prostate biopsy. Any additional hospitalization due to other diseases was not included in the data analysis. The length of hospital stay was defined as the total number of days spent in the hospital, excluding hospitalized time due to medical conditions other than the TRUS-guided biopsy. Non-infectious complications after the procedure included pain, hematuria, hematospermia, rectal bleeding, and acute urinary retention (AUR). The intensity of pain was measured on the evening of the biopsy using the numeric pain rat-

Table 2. Comparison among three groups with respect to post-procedural infectious complications, re-hospitalization, and mean length of hospital stay

	Group I (N = 165)	Group II (N = 116)	Group III (N = 170)	*P*-value
Overall infectious complications (%)	36 (21.8)	13 (11.2)	11 (6.5)	< .001
Asymptomatic bacteriuria/pyuria	7 (4.2)	9 (7.8)	4 (2.4)	.092
UTI or prostatitis without fever	13 (7.9)	1 (0.9)	6 (3.5)	.015
UTI or prostatitis with fever	10 (6.1)	1 (0.9)	0 (0)	.001
Bacteremia or sepsis or SIRS	6 (3.6)	2 (1.7)	1 (0.6)	.133
Re-hospitalization (%)	16 (9.7)	3 (2.6)	1 (0.6)	< .001
Mean length of hospital stay, days; mean ± SD	3.42 ± 1.43	3.22 ± 1.41	3.04 ± 0.54	.012

Abbreviations: UTI, Urinary Tract Infection; SIRS, Systemic Inflammatory Response Syndrome.

Table 3. Comparison among three groups with respect to post-procedural non-infectious complications

	Group I (N = 165)	Group II (N = 116)	Group III (N = 170)	*P*-value
Pain, NPRS; mean ± SD	1.64 ± 0.86	1.54 ± 0.96	1.49 ± 0.62	.211
Hematuria (%)	47 (28.5)	41 (35.3)	45 (26.5)	.254
Hematospermia (%)	1 (0.6)	1 (0.6)	0 (0)	.518
Rectal bleeding (%)	4 (2.4)	4 (3.4)	2 (1.2)	.429
AUR (%)	5 (3)	8 (6.9)	2 (1.2)	.029

Abbreviations: NPRS, Numeric Pain Rating Scale; AUR, Acute Urinary Retention.

ing scale (NPRS), with an 11-point numeric scale ranging from '0' representing 'no pain' to '10' representing 'worst pain imaginable'.[15] Other non-infectious complications were defined as events that developed at any time during the follow-up period of one month.

Statistical Analysis

Comparison of the incidence of post-procedural complications, re-hospitalization rates, and length of hospital stay among the three groups according to the method of rectal cleansing were assessed using one-way ANOVA for continuous variables and the Pearson Chi-square test for categorical variables. Multiple logistic regression analysis was performed to estimate adjusted odds ratios (ORs) to investigate which factors among the baseline clinical characteristics (rectal cleansing method, age, prostate volume, DM, Foley catheter insertion, recent antimicrobial use, recent hospitalization, recent history of UTI, prostatitis, prostate biopsy, and FQ resistance) significantly influenced the incidence of post-procedural infectious complications and re-hospitalization rates. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). A *P* value less than 0.05 was considered significant.

RESULTS

A total of 451 patients enrolled in this study were divided into Group I (n = 165), II (n = 116), and III (n = 170), respectivey. The mean age of the patients was 68.28 ± 8.38 years, the mean prostate volume was 41.17 ± 22.38 cc, and the median PSA level (interquatile range) was 6.5 (4.1-10.8) ng/mL. According to the biopsy, the final diagnosis was benign prostate hyperplasia (n=237, 52.5%), prostate cancer (n = 192, 42.6%), atypical small acinar proliferation (ASAP) (n = 16, 3.5%), and others (n=6, 1.3%). The results of the rectal swab culture performed before the biopsy were E. coli (n = 397, 88%), K. pneumonia (n=15, 3.3%), others (n=22, 4.9%), and no bacterial growth (n=17, 3.8%). Overall, FQ resistance was observed in 197 (43.7%) patients. The demographics and clinical characteristics of the patients were compared among the three groups based on a method of rectal cleansing (**Table 1**). The mean prostate volume was significantly smaller in group III than in groups I and II (*P* = .001). The incidence of chronic kidney disease was different among the three groups (*P* = .025). Meanwhile, there were no statistically significant differences among the three groups in terms of age, PSA level, DM, Foley catheter insertion state, recent antimicrobial use, recent hospitalization, recent history of UTI or prostatitis, recent history of prostate biopsy, and biopsy results.

Overall, post-procedural infectious complications occurred in 60 (13.3%) of 451 patients, among which 36 (21.8%), 13 (11.2%), and 11 (6.5%) cases developed in groups I, II, and III, respectively (*P* < .001) (**Table 2**). The incidence of overall post-procedural infectious complications was significantly lower in groups II (*P* = .025) and III (*P* < .001) than group I. However, there was no significant difference between groups II and III. Infectious complications consisted of asymptomatic bacteriuria or pyuria (n = 20, 4.4%), UTI or prostatitis without fever (n = 20, 4.4%), UTI or prostatitis with fever (n = 11, 2.4%), bacteremia, sepsis, or SIRS (n = 9, 2%). *E. coli* was the cause of bacteremia in all cases (n = 9), among which 50% were FQ-resistant *E coli*. Among various post-procedural infectious complications, UTI or prostatitis occurred more frequently in group I than in groups II and III.

Re-hospitalization rates were 9.7%, 2.6%, and 0.6% in groups I, II, and III, respectively (*P* < .001). Sub-group

Table 4. Influence of various clinical characteristics on post-procedural infectious complications

	OR	*P*-value	95% CI
Rectal cleansing methoda			
Group II	0.472	.038	0.232–0.958
Group III	0.267	< .001	0.129–0.555
Age	1.013	.527	0.974–1.053
Prostate volume	0.994	.377	0.980–1.008
Diabetes Mellitus	0.806	.587	0.369–1.757
Chronic kidney disease	2.075	.112	0.844–5.099
Foley catheter insertion state	5.509	.016	1.380–22.001
Recent antimicrobial use	1.036	.943	0.392–2.737
Recent hospitalization 1	.026	.964	0.343–3.068
Recent history of UTI or prostatitis	1.962	.263	0.603–6.388
Recent history of prostate biopsy	2.638	.407	0.266–26.124
FQ resistance	0.873	.662	0.474–1.608

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; UTI, Urinary Tract Infection; FQ, Fluoroquinolone.
aThe reference category is Group I.

Table 5. Influence of various clinical characteristics on re-hospitalization rates

	OR	*P*-value	95% CI
Rectal cleansing measurea			
Group II	0.247	.029	0.070–0.869
Group III	0.055	.005	0.007–0.421
Age	0.975	.448	0.914–1.040
Prostate volume	0.970	.055	0.941–1.001
Diabetes Mellitus	2.482	.135	0.753–8.184
Chronic kidney disease	2.049	.369	0.429–9.789
Foley catheter insertion state	0.455	.628	0.019–11.001
Recent antimicrobial use	0.745	.698	0.167–3.331
Recent hospitalization	0.922	.926	0.166–5.114
Recent history of UTI or prostatitis	5.934	.006	1.660–21.214
Recent history of prostate biopsy	19.024	.030	1.322–273.824
FQ resistance	1.232	.697	0.432–3.513

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; UTI, Urinary Tract Infection; FQ, Fluoroquinolone.
aThe reference category is Group I.

analysis showed that there were significant differences between groups I and II ($P = .028$) and groups I and III ($P < .001$). However, there was no significant difference between groups II and III. The mean length of hospital stay was 3.42 ± 1.43 days, 3.22 ± 1.41 days, and 3.04 ± 0.54 days in groups I, II, and III, respectively. While the mean hospital stay was significantly longer in group I than in group III ($P = .009$), there was no significant difference between groups I and II and groups II and III. Regarding non-infectious post-procedural complications, the overall NPRS was 1.56 ± 0.81. The incidence of hematuria, hematospermia, rectal bleeding, and AUR after TRUS biopsy was 29.5% (n = 133), 0.4% (n = 2), 2.2% (n = 10), and 3.3% (n = 15), respectively (**Table 3**). Among these non-infectious complications, the incidence of AUR was significantly lower in group III than II ($P = .029$). However, there were no significant differences among the three groups in terms of other non-infectious complications.

Among the various clinical characteristics including rectal cleansing method, age, prostate volume, DM, Foley catheter insertion, recent antimicrobial use, recent hospitalization, recent history of UTI, prostatitis, prostate biopsy, and FQ resistance, the rectal cleansing method and Foley catheter insertion were significant factors for the occurrence of post-procedural infectious complication (**Table 4**). The incidence of post-procedural infectious complications was significantly reduced in group II (OR = 0.472, 95% CI: 0.232-0.958, $P = .038$) and group III (OR = 0.267, 95% CI: 0.129-0.555, $P < .001$) as compared to group I. In addition, Foley catheter insertion state (OR = 5.509, 95% CI: 1.380-22.001, $P = .016$) was an independent predictor of infectious complications after TRUS biopsy. Meanwhile, re-hospitalization rates were significantly influenced by the rectal cleansing method, recent history of UTI or prostatitis, and recent history of prostate biopsy (Table 5). Among the three groups, re-hospitalization rates were significantly lower in group II (OR = 0.247, 95% CI: 0.070-0.869, $P = .029$) and group III (OR = 0.055, 95% CI: 0.007-0.421, $P = .005$) than in group I.

DISCUSSION

The human gastrointestinal tract normally harbors numerous microbiomes, and the highest concentration of microbiomes is present in the rectum. Damage to the barrier function of the rectal mucosa can result in entrance of viable rectal microbiomes and their virulent products into systemic circulation, which may result in sepsis, SIRS, multiple organ dysfunction syndrome, and even death. This phenomenon is called “bacterial translocation”, and various rectal procedures and operations can facilitate translocation of normal microbiomes.[16] However, exactly how the bacterial colonies from the rectum enter directly into the bloodstream, urine, or prostate tissue through the biopsy needle and lead to infectious complications remains to be elucidated.

Several studies comparing transperineal and transrectal prostate biopsy have suggested that these rectal microbiomes may be closely related to the infectious complications of prostate biopsy.[3,17] The transperineal route for prostate biopsy, which represents an alternative pathway to avoid direct contact with the rectal microbiome, has shown a significantly lower incidence of infectious complications compared to the typical transrectal route.[3] According to a study by Grummet el al., the rate of re-hospitalization for infection was zero among 245 patients.[17] Furthermore, a systemic review of the literature published from 2003 to 2013 found that transperineal prostate biopsy resulted in only a 0.076% re-hospitalization rate for sepsis,[17] which is significantly lower than that reported for transrectal prostate biopsy.[3,4] However, despite the advantage of a decreased rate of serious infectious complications, transperineal prostate biopsy is not widely used because it is difficult to perform under local anesthesia and incurs relatively higher costs, and requires specialized equipment.[17] Therefore, methods that have the potential to minimize the effect of rectal microbiomes in transrectal prostate biopsy are relatively preferred.

Several studies reported that bowel preparation using a disinfectant agent such as povidone-iodine significantly reduced post-procedural infectious complications,[11,18,19] including a previous study showing that rectal cleansing with povidone-iodine effectively reduced the colony count of rectal microbiomes including FQ-resistant *E.coli* owing to its bactericidal activity.[19] Moreover, as compared to antibiotic prophylaxis alone, rectal cleansing using povidone-iodine in addition to antibiotic prophylaxis was shown to be more effective in lowering the incidence of infectious complications following prostate biopsy.[3,5,20] However, a prospective randomized trial reported that although rectal cleansing with povidone-iodine before TRUS-guided prostate biopsy had led to a 42% decrease in the relative risk of post-procedural infectious complications, it was not

statistically significant.[13] Currently, American Urological Association (AUA) and European Association of Urology guidelines recommend rectal cleansing with povidone-iodine plus antibiotic prophylaxis before transrectal prostate biopsy if the local risk of infectious complications is high.[3,21] Regarding the rectal cleansing protocol, a variety of pre-procedural rectal preparation methods have been used thus far.[11-13,18,19,22] Ghafoori et al. demonstrated that the injection of povidone-iodine solution into the rectum significantly decreased the rate of post-procedural infectious complications.[11] A study by Park et al. claimed that soaking the rectum with a povidone-iodine suppository was more effective than a povidone-iodine enema.[19] Chen et al. adopted a direct method of cleansing the rectal mucosa overlying the prostate gland using povidone-iodine gauze that showed a 9.6% reduction in the incidence of post-procedural infectious complications.[22] Another study reported that this direct cleansing of the rectal vault and perianal area by povidone-iodine reduced the rate of post-procedural infectious complications by decreasing rectal microbial colonization.[18] In our study, we compared the effectiveness of three rectal cleansing methods for reducing post-procedural infectious complications. The incidence of post-procedural infectious complications and re-hospitalization rates were lowest in patients who underwent direct manual cleansing of the mucosal surface of the anus and lower rectum using forceps and povidone-iodine cotton balls. Additionally, this group of patients showed the shortest mean length of hospital stay. Thus, our results may positively support the expectation that, among various rectal cleansing methods, direct manual rectal cleansing may be the most effective way to yield a bactericidal effect and decrease rectal microbial colonization before TRUS-guided prostate biopsy.

Prophylactic antibiotics is one of the well-known methods of minimizing infectious complications caused by rectal microbiomes in TRUS-guided prostate biopsy.[23,24] According to AUA guidelines, antibiotic prophylaxis is recommended in all patients.[23] In general, FQ antibiotics are the most preferable choice of drugs.[21] Since *E. coli* is the etiology of most infectious complications following prostate biopsy, the selection of prophylactic antibiotics focuses on this bacteria.[25] However, despite FQ-based prophylaxis, a noticeable increase in the prevalence of multi-resistant organisms including FQ-resistant organisms has recently been reported, which has contributed to the increased incidence of infectious complications.[26] Therefore, the need for a new prophylactic antibiotics regimen has arisen.

Currently, targeted antibiotics prophylaxis using a rectal swab is considered one of the more effective regimens.[29,30] According to a meta-analysis, the incidence of infectious complications following transrectal prostate biopsy in the targeted antibiotic prophylaxis group was lower than in the empirical group.[31] However, the usefulness of targeted prophylaxis in preventing post-procedural infectious complications remains controversial. A study by Liss et al. found no significant difference in the rate of sepsis between groups receiving targeted prophylaxis versus empirical prophylaxis,[32] and all of the causative organisms of sepsis after prostate biopsy were FQ-sensitive *E. coli* despite adequate FQ prophylaxis. In our study, the causative organisms of sepsis were always *E coli*, of which only 50% were FQ-resistant *E coli*. Based on these results, it can be assumed that FQ prophylaxis for FQ-sensitive *E. coli* found in the rectal flora does not always prevent sepsis. Further investigations are necessary to determine which virulence factors besides FQ resistance are involved in post-biopsy sepsis despite sufficient antibiotic prophylaxis.[33,34]

Recent urinary catheterization is one of the known risk factors for post-procedural infectious complications. Simsir et al. reported that the presence of a urinary catheter had predictive risk value for sepsis following TRUS-guided prostate biopsy because the catheter can become an important mediator of microbial colonization.[35] In our study, recent urinary catheterization increased the risk of overall infectious complications by five-fold. However, given that it is frequently used for short periods of time in most clinical situations, the urinary catheter may be more typically associated with minor infectious complications such as bacteriuria.[36]

In our study, the mean prostate volume was significantly smaller in group III. Therefore, there would be a possibility that a difference in baseline prostate size could produce bias or influence on the rate of postprocedural infectious complications. However, in multivariate analysis in our study, no significant association between the prostate volume and infectious complications was found. This result is in agreement with other studies.[3,26]

Our study has several limitations. First, the study design was retrospective. Therefore, it was difficult to definitively assure that all patients underwent the same follow-up assessment. And also, future studies including a randomized clinical trial are needed to validate our results. Second, although urinalysis was performed in all patients, additional evaluation including urine culture, blood culture, or other laboratory studies were performed only in symptomatic patients. Thus, those who were asymptomatic or had mild symptoms did not undergo these additional studies.

CONCLUSIONS

Combined with targeted antimicrobial prophylaxis, direct manual cleansing of the mucosal surface of the anus and lower rectum using povidone-iodine cotton balls was most effective in preventing post-procedural infectious complications among the three different rectal cleansing methods.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

REFERENCES

1. Shariat SF, Roehrborn CG. Using biopsy to detect prostate cancer. Rev Urol. 2008;10:262-80.
2. Liss MA, Ehdaie MB, Loeb S, et al. An update of the American Urological Association white paper on the prevention and treatment of the more common complications related to

prostate biopsy. J Urol. 2017;198:329-34.

3. Walker JT, Singla N, Roehrborn CG. Reducing infectious complications following transrectal ultrasound-guided prostate biopsy: a systematic review. Rev Urol. 2016;18:73-89.
4. Ryu JW, Jung SI, Ahn JH, et al. Povidone-iodine rectal cleansing and targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound-guided prostate biopsy are associated with reduced incidence of postoperative infectious complications. Int Urol Nephrol. 2016;48:1763-70.
5. Loeb S, van den Heuvel S, Zhu X, Bangma CH, Schröder FH, Roobol MJ. Infectious complications and hospital admissions after prostate biopsy in a European randomized trial. Eur Urol. 2012;61:1110-4.
6. Loeb S, Carter HB, Berndt SI, Ricker W, Schaeffer EM. Complications after prostate biopsy: data from SEER-Medicare. J Urol. 2011;186:1830-4.
7. Loeb S, Vellekoop A, Ahmed HU, et al. Systematic review of complications of prostate biopsy. Eur Urol. 2013;64:876-92.
8. Valverde A, Msika S, Kianmanesh R, et al. Povidone-iodine vs sodium hypochlorite enema for mechanical preparation before elective open colonic or rectal resection with primary anastomosis: a multicenter randomized controlled trial. Arch Surg. 2006;141:1168-74.
9. Williamson DA, Barrett LK, Rogers BA, Freeman JT, Hadway P, Paterson DL. Infectious complications following transrectal ultrasound–guided prostate biopsy: new challenges in the era of multidrug-resistant Escherichia coli. Clin Infect Dis. 2013;57:267-74.
10. Pu C, Bai Y, Yuan H, et al. Reducing the risk of infection for transrectal prostate biopsy with povidone–iodine: a systematic review and meta-analysis. Int Urol Nephrol. 2014;46:1691-8.
11. Ghafoori M, Shakiba M, Seifmanesh H, Hoseini K. Decrease in infection rate following use of povidone-iodine during transrectal ultrasound guided biopsy of the prostate: a double blind randomized clinical trial. Iran J Radiol. 2012;9:67-70.
12. Raman JD, Lehman KK, Dewan K, Kirimanjeswara G. Povidone iodine rectal preparation at time of prostate needle biopsy is a simple and reproducible means to reduce risk of procedural infection. J Vis Exp. 2015:e52670.
13. AbuGhosh Z, Margolick J, Goldenberg SL, et al. A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy. J Urol. 2013;189:1326-31.
14. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992;101:1644-55.
15. Jensen MP, McFarland CA. Increasing the reliability and validity of pain intensity measurement in chronic pain patients. Pain. 1993;55:195-203.
16. Roy J, Gatt M. Causes of surgical sepsis including bacterial translocation. Surgery. 2012;30:645-50.
17. Grummet JP, Weerakoon M, Huang S, et al. Sepsis and 'superbugs': should we favour the transperineal over the transrectal approach for prostate biopsy? BJU Int. 2014;114:384-8.
18. Gyorfi JR, Otteni C, Brown K, et al. Peri-procedural povidone-iodine rectal preparation reduces microorganism counts and infectious complications following ultrasound-guided needle biopsy of the prostate. World J Urol. 2014;32:905-9.
19. Park DS, Oh JJ, Lee JH, Jang WK, Hong YK, Hong SK. Simple use of the suppository type povidone-iodine can prevent infectious complications in transrectal ultrasound-guided prostate biopsy. Adv Urol. 2009;2009:750598.
20. Hwang EC, Jung SI, Seo YH, et al. Risk factors for and prophylactic effect of povidone-iodine rectal cleansing on infectious complications after prostate biopsy: a retrospective cohort study. Int Urol Nephrol. 2015;47:595-601.
21. Mottet N, Bellmunt J, Briers E, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol. 2017;71:618-29.
22. Chen P, Chang C, Wang B-F, et al. Standardized protocol in preventing postoperative infectious complications after transrectal ultrasound-guided prostate biopsy: a retrospective study of 246 patients. Urol Sci. 2016;27:140-3.
23. Wolf JS, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol. 2008;179:1379-90.
24. Zani EL, Clark OAC, Rodrigues Netto Jr N. Antibiotic prophylaxis for transrectal prostate biopsy. Cochrane Database Syst Rev. 2011;5:CD006576.
25. Katouli M. Population structure of gut Escherichia coli and its role in development of extra-intestinal infections. Iran J Microbiol. 2010;2:59-72.
26. Wagenlehner FM, Van Oostrum E, Tenke P, et al. Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, a prospective multinational multicentre prostate biopsy study. Eur Urol. 2013;63:521-7.

27. Cuevas O, Oteo J, Lázaro E, et al. Significant ecological impact on the progression of fluoroquinolone resistance in Escherichia coli with increased community use of moxifloxacin, levofloxacin and amoxicillin/clavulanic acid. J Antimicrob Chemother. 2011;66:664-9.
28. Carignan A, Roussy JF, Lapointe V, Valiquette L, Sabbagh R, Pépin J. Increasing risk of infectious complications after transrectal ultrasound–guided prostate biopsies: time to reassess antimicrobial prophylaxis? Eur Urol. 2012;62:453-9.
29. Taylor AK, Zembower TR, Nadler RB, et al. Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol. 2012;187:1275-9.
30. Duplessis CA, Bavaro M, Simons MP, et al. Rectal cultures before transrectal ultrasound-guided prostate biopsy reduce post-prostatic biopsy infection rates. Urology. 2012;79:556-61.
31. Roberts MJ, Williamson DA, Hadway P, Doi SA, Gardiner RA, Paterson DL. Baseline prevalence of antimicrobial resistance and subsequent infection following prostate biopsy using empirical or altered prophylaxis: a bias-adjusted meta-analysis. Int J Antimicrob Agents. 2014;43:301-9.
32. Liss MA, Kim W, Moskowitz D, Szabo RJ. Comparative effectiveness of targeted vs empirical antibiotic prophylaxis to prevent sepsis from transrectal prostate biopsy: a retrospective analysis. J Urol. 2015;194:397-402.
33. Liss MA, Johnson JR, Porter SB, et al. Clinical and microbiological determinants of infection after transrectal prostate biopsy. Clin Infect Dis. 2015;60:979-87.
34. Vaezjalali M, Azimi H, Hosseini SM, Taghavi A, Goudarzi H. Different strains of BK polyomavirus: VP1 sequences in a group of Iranian prostate cancer patients. Urol J. 2018;15(2):44-8.
35. Simsir A, Kismali E, Mammadov R, Gunaydin G, Cal C. Is it possible to predict sepsis, the most serious complication in prostate biopsy? Urol Int. 2010;84:395-9.
36. Nicolle LE. Catheter associated urinary tract infections. Antimicrob Resist Infect Control. 2014;3:23.