

# Incidence of Fluoroquinolone Resistant Aerobic Organisms and Efficacy of Rectal Cleaning in Men Undergoing Transrectal Ultrasound Guided Prostate Biopsy

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**Objective:** To evaluate the incidence of fluoroquinolone resistant organisms in rectum and efficacy of rectal cleansing in men undergoing transrectal ultrasound guided prostate biopsy (TRUS-Bx) in Ramathibodi Hospital.

**Material and Method:** Between December 2012 and March 2013, 105 male patients who had prostate specific antigen (PSA) more than 4 ng/ml or abnormal digital rectal examination (DRE) underwent TRUS-Bx were enrolled. Two specimens of rectal swab for bacterial culture were taken from each patient. The first rectal swab was obtained at the beginning of the procedure (BC), another after cleaning the rectum with betadine solution (AC). All gram-negative enteric bacteria were isolated. The results of both specimens were analyzed by Chi-square test and McNemar test.

**Results:** One hundred five men that underwent TRUS-Bx were included in the present study. Of the 105 patients, 15 men were found to have no bacterial growth while 90 men showed bacterial growth at the BC procedure. After the AC procedure, 53 men (59%) remained having positive culture for bacterial strains ( $p < 0.001$ ), and 37 (41%) showed no bacterial growth. There was no change in the bacterial strains in 36 men while another four men demonstrated an increasing number of bacterial strains at the AC stage. Of 90 patients, 81 (90%) men carried ciprofloxacin resistant organisms including *Escherichia coli* (*E. coli*) (55.56%), extended-spectrum  $\beta$ -lactamase (ESBL)-producing *E. coli* (35.80%), *Klebsiella pneumoniae* (6.17%), and *Enterobacter cloacae* (2.47%).

**Conclusion:** Incidence of fluoroquinolone resistant organisms in rectum of men undergoing TRUS-Bx at Ramathibodi Hospital was approximately 90%. *E. coli* was the most common organism. The results indicated that rectal cleaning significantly decreases the incidence of overall bacterial colonization in rectum before TRUS-Bx.

**Keywords:** Fluoroquinolone resistant, Prostate biopsy, Prostate cancer, TRUS-Bx infection

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Prostate cancer is one of the most common cancers in elderly men<sup>(1)</sup>. Before the prostate specific antigen (PSA) era, most of prostate cancer patients were diagnosed at a late stage. Stage migration from advanced stage to more early stage has been observed after the booming of PSA screening. In 2012, the incidence of prostatic cancer in the United States was 29%<sup>(2)</sup>. There were 241,740 new cases and 28,170 deaths in that year<sup>(2)</sup>. The prevalence of prostate cancer in northeastern Thailand in 2012 was 6.2%<sup>(3)</sup>. Early detection of prostate cancer included PSA checking

and digital rectal examination (DRE). In case of abnormal DRE or high level of PSA, transrectal ultrasound guided prostate biopsy (TRUS-Bx) will be advised to the patients for tissue diagnosis. Because the biopsy needle must be passed through rectal mucosa before reaching the prostate gland, one of the most serious complications is infection, including urinary tract infection (UTI) caused by epididymo-orchitis, acute prostatitis, etc. These complications may lead to bacteremia, severe septicemia, and even death.

Contamination of rectal flora into the prostate tissue and blood stream is the major pathogenesis of urinary tract infection after procedure. The most common organism responsible for these infectious complications is *Escherichia coli*<sup>(4-9)</sup>. Until now, there is no standard protocol for preoperative patient preparation and antibiotic prophylaxis.

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Fluoroquinolones are most commonly used for preoperative antibiotic prophylaxis due to high drug level in the prostate tissue<sup>(15)</sup>.

Previous study has shown that fluoroquinolone prophylaxis can significantly decrease infection rate of this procedure<sup>(17,18)</sup>. However, recent studies have highlighted an increasing trend of infectious complications due to fluoroquinolone resistant organisms<sup>(10,11)</sup>. The incidence of fluoroquinolone resistant organisms was approximately 20% in men who underwent TRUS-Bx<sup>(10,11)</sup>. Furthermore, there were several previous studies suggested cleansing the rectum with 10% povidone-iodine solution<sup>(12-14)</sup>. However, most of them are not randomized controlled trial studies<sup>(12-14)</sup>.

Each year, we have more than 200 patients undergoing TRUS-Bx. In 2012, four patients came back with sepsis complications (unpublished data). Blood cultures and urine cultures showed *E. coli* in these patients. Though these infections were infrequent, some patients developed hemodynamic instability leading to high morbidity and mortality. The objective of the present study was to evaluate the incidence of fluoroquinolone resistant organisms in elderly men underwent TRUS-Bx, as well as to evaluate the efficacy of rectal cleansing before performing TRUS-Bx in this group of patients at Ramathibodi Hospital.

### Material and Method

Following the Ethical Review Committee approval of the study (ID 09-55-30), we enrolled elderly men (older than 50 year) with PSA greater than 4 ng/ml or abnormal DRE who were to undergo TRUS-Bx between December 2012 and March 2013. All patients signed the informed consent at the outpatient clinic. The patient who had history of bowel disease such as colorectal cancer, post radiation, post bowel surgery and immunocompromised host such as diabetes mellitus, or human immunodeficiency virus infection were excluded.

The patients received oral ciprofloxacin 500 mg twice daily, starting one day before the procedure. They were advised to have a cleansing enema at home one night before the procedure. This method is the routine regimen of Ramathibodi Hospital. In the operating room, the patients were placed in the lithotomy position, proctoscope was applied, and first rectal swab was obtained from the anal canal. Then rectum was cleaned with 50 ml of NSS plus 10% povidone-iodine solution. After five minutes, second

rectal swab was obtained again. Finally, 12 cores TRUS-Bx were performed in a standard manner. The flow chart was shown in Fig. 1. All patients were advised to continue the oral ciprofloxacin for two days. All specimens were sent to the microbiological lab to isolate gram negative enteric bacteria. The swabs were cultured on blood agar plates, incubated at 35 to 37°C in a CO<sub>2</sub> incubator.

We identified infectious complications within 30 days after the procedure using telephone contact and follow-up database from electronic medical records. All data were analyzed. The patients were grouped accordingly to culture results, which were positive or negative for fluoroquinolone resistant bacteria. These groups were compared before and after rectal cleansing. Standard statistical methods were performed with SPSS version 18 (IBM Corp., Armonk, NY, USA), including the Chi-square test and McNemar test for significance, with  $p < 0.05$  indicating statistical significance.

### Results

One hundred five men were enrolled in the present study. Mean age of the patients was 62.6 year (50-89 year). Fourteen patients (13.3%) did not have other comorbidity, 26 patients had dyslipidemia, 47 had hypertension, nine had coronary artery disease, and other nine had history of cerebrovascular accident. We excluded diabetic and other immunocompromised patients because these conditions may alter organisms in rectum. Before rectal cleansing, we found bacterial growth in 90 men and only 15 men showed no growth (Fig. 1). After rectal cleansing, 15 men still showed no growth, 13 of 90 men (14.5%) showed reduction of bacterial growth, 36 men (40%) showed no change, and four men (4.5%) showed an increase. Interestingly, 37 of 90 men (41%) showed bacterial disappearance. There was significant decrease in the number of patients

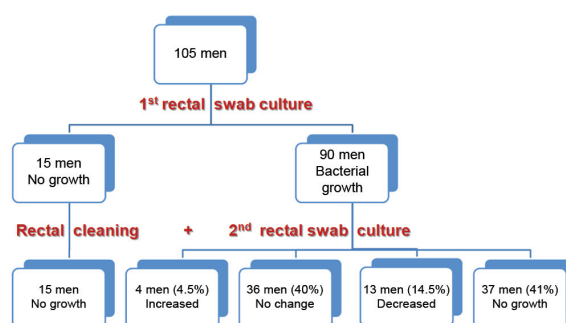


Fig. 1 Results of rectal swab culture after rectal cleansing.

**Table 1.** Comparison of bacterial growth between two groups

	Before rectal cleansing (n = 105)	After rectal cleansing (n = 105)	p-value
No. patients had bacterial growth	90 (85.7%)	53 (50.5%)	<0.001
No. patients had no bacterial growth	15 (14.3%)	52 (49.5%)	<0.001

who had bacterial growth after rectal cleansing ( $p < 0.001$ ) as shown in Table 1.

Ciprofloxacin sensitivity was shown in Fig. 2. Among 90 men who had bacterial growth, 81 men had ciprofloxacin resistant organism. This was approximately 90%. Only nine men were sensitive to ciprofloxacin. From the 81 men who had ciprofloxacin resistant organism (Fig. 3), we found 55.56% of *E. coli*, 35.80% of extended-spectrum  $\beta$ -lactamase (ESBL)-producing *E. coli*, 6.17% of *Klebsiella pneumoniae*, and 2.47% of *Enterobacter cloacae*. As shown in Fig. 4, 81 of 90 men (90%) had ciprofloxacin resistant organism before rectal cleansing; and after rectal cleansing and 44 from 53 men (83.02%) remained positive for ciprofloxacin resistant organism after rectal cleaning. The reduction rate was 7%.

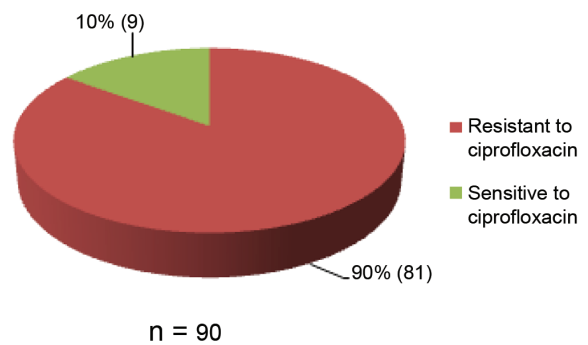
After TRUS-Bx, five patients were lost to follow-up and could not be contacted by telephone. Four of 100 men (4%) had fever one day after the procedure but spontaneously resolved without seeing the doctor. In all of these patients, rectal swab culture showed ciprofloxacin resistant organisms including ESBL-*E. coli*, *Klebsiella*, and *Enterobacter*. The other one patient (1%) developed fever 14 days after the procedure; however, his blood culture showed no bacterial growth. Pre-operative rectal swab culture also showed *E. coli* resistant to ciprofloxacin. There was one patient (1%) who developed clinical sepsis. He was admitted at Ramathibodi Hospital, blood and urine cultures showed ESBL-*E. coli* resistant to ciprofloxacin, and it was the same organism from his rectal swab culture.

**Discussion**

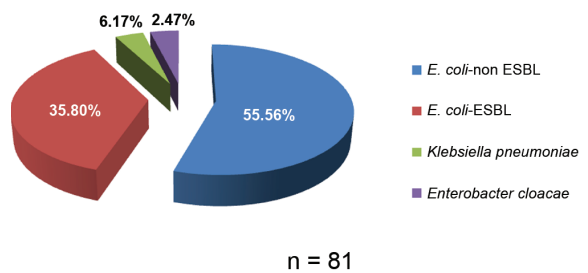
To date, the optimal drug for antimicrobial prophylaxis before TRUS-Bx remains an unresolved issue. Fluoroquinolone antibiotics are commonly used for antibiotic prophylaxis based on achievable concentration in prostate and rectal tissue<sup>(15)</sup>. The American Urological Association best practice statement for antibacterial prophylaxis recommends to use fluoroquinolone as a first-line antimicrobial prophylaxis before TRUS-Bx<sup>(16)</sup>. In our center, we have also used ciprofloxacin as an antibiotic prophylaxis

because of its cost-effectiveness and its high drug level in the prostatic tissue.

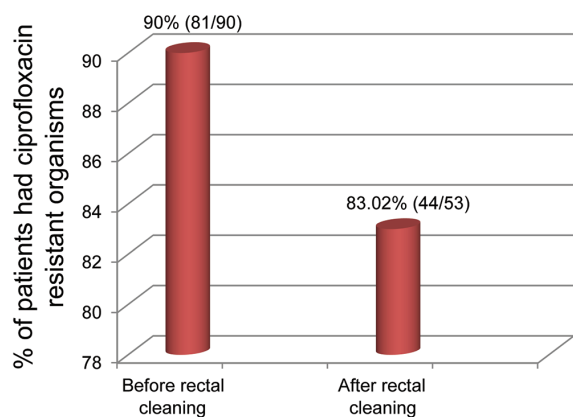
Prior studies have demonstrated that the incidence of infectious complications is very low in patients who have received fluoroquinolone



**Fig. 2** Proportion of ciprofloxacin sensitivity.



**Fig. 3** Type of ciprofloxacin resistant organisms.



**Fig. 4** The effect of rectal cleaning to ciprofloxacin resistant organisms.

prophylaxis<sup>(17,18)</sup>. The infection rates significantly decrease from 25% to 2 to 8%<sup>(17,18)</sup>. Sepsis after TRUS-Bx have been reported between 0.1 to 2.2% among patients undergoing empirical prophylaxis with fluoroquinolone<sup>(19,20)</sup>. For patients who had septic shock and death after TRUS-Bx, ciprofloxacin resistant *E. coli* was reported as the main causative organism<sup>(21)</sup>. Several recent studies have highlighted an increasing trend of infectious complications due to fluoroquinolone resistant organisms. The incidence of fluoroquinolone resistant organisms from rectal swab cultures was approximately 20% in men who underwent TRUS-Bx<sup>(10,11)</sup>.

However, the true incidence of fluoroquinolone resistant organisms in the general population is not known. From our study, we found that the incidence was higher than that in previous other studies (90% vs. 20%)<sup>(10,11)</sup>. Taylor et al used rectal swab cultures within few days prior TRUS-Bx and selected antibiotic prophylaxis depending on sensitivity results<sup>(10)</sup>. The benefit of this technique was that the patients would receive specific antibiotic from their sensitivity results. However, this technique might not be practical in Thailand, because the patients would be inconvenience from one more DRE and more hospital visit before TRUS-Bx. This technique does not match for a high volume patients hospital. Moreover, the positive culture for fluoroquinolone resistant organisms does not lead to post-procedural infection in all patients. Rectal cleaning is easier and more practical methods.

Rectal cleansing is safe and easy to perform, minimal time consuming and inexpensive procedure. It is more practical than pre-procedure rectal swab cultures for antimicrobial prophylaxis. From our present study, bacterial colonization in rectum could be significantly reduced after rectal cleansing ( $p < 0.001$ ). However, the clinical benefit from routine rectal cleansing such as post-operative infectious complications still needs further study.

Based on our study, 44 patients were colonized with ciprofloxacin resistant organisms after rectal cleansing. All of these men had higher risk of post-operative infection. Surprisingly, only six patients (13.64% of expected) experienced post-operative fever. A possible explanation was that there were other factors associated with post-operative infection apart from resistant organisms such as immune status of patients, degree of contaminations and amount of resistant organisms. There was only one patient developed clinical sepsis in our study. Blood culture and rectal swab culture showed the same resistant organism.

Resistant organisms in rectum may be related to infectious complications after TRUS-Bx.

Because rectal cleansing could significantly reduce bacterial colonization in the rectum without increasing morbidity to the patients, we recommend routine rectal cleansing in all patients subjected to TRUS-Bx. Even with a high incidence of ciprofloxacin resistant organisms, we cannot recommend using new broad-spectrum antibiotics instead of ciprofloxacin due to a small number of patients and low incidence of post-procedural infection. However, broad-spectrum antibiotic prophylaxis or targeted antibiotic prophylaxis will be benefit to immunocompromised patients before performing TRUS-Bx.

The present study had several limitations. The power of this study was limited by the small number of patients and no controlled arm. Furthermore, the impact of rectal cleansing may be different if we could perform anaerobic bacterial culture. However, this was limited by the research fund. Finally, the present study was conducted based on the high incidence of fluoroquinolone resistant organisms in our hospital. The results may be different in other hospitals having low incidence of drug resistant organisms. Further prospective large scale randomized controlled studies are needed to confirm our findings.

## Conclusion

Incidence of the fluoroquinolone resistant organisms in men underwent TRUS-Bx at Ramathibodi Hospital was approximately 90%. *E. coli* was the most common organism. Rectal cleansing significantly decreased the incidence of overall bacterial colonization in rectum before performing TRUS-Bx. However, clinical significant from rectal cleaning and antimicrobial prophylaxis regimen alteration should be evaluated further with larger randomized controlled trials.

## What is already known on this topic?

One of the serious complications after TRUS-Bx is infection. Sepsis after TRUS-Bx have been reported between 0.1 to 2.2%. Although fluoroquinolone is recommended for antimicrobial prophylaxis before the procedure, but previous published foreign studies found that there was an increasing trend of infectious complications due to fluoroquinolone resistant organisms. The incidence of fluoroquinolone resistant organisms from rectal swab cultures was approximately 20% in men who underwent TRUS-Bx. The true incidence of



fluoroquinolone resistant organisms in Thai men who underwent TRUS-Bx was not clear. Furthermore, rectal cleaning with povidone-iodine solution is simple technique that might be effective to decrease bacterial colonization in the rectum. Most of previous studies in this topic were small and not randomized.

#### What this study adds?

The incidence of fluoroquinolone resistant organisms in rectum of Thai men who underwent TRUS-Bx in Ramathibodi Hospital was very high (90%). Rectal cleansing significantly reduced overall bacterial colonization in rectum before performing TRUS-Bx. However, further large randomized studies are needed to prove clinical significance of rectal cleansing and infectious complications after the procedure.

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#### Potential conflicts of interest

None.

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อุบัติการณ์ของเชื้อก่อโรคที่ฟุ้งออกซิเจนที่ดื้อต่อยากลุ่ม *fluoroquinolone* จากการตรวจเพาะเชื้อในทวารหนักและประสิทธิภาพของการสวนล้างทวารหนัก ในกลุ่มผู้ชายที่ถูกตรวจชิ้นเนื้อหามะเร็งต่อมลูกหมาก

ประกาศกร กังอุบล, พิทักษ์ สันตนิรันดร์, ปกเกศ ศิริศรีตรีรักษ์, วิทย์ วิเศษสินธุ์, เปรมสันต์ สังข์คุ้ม

**วัตถุประสงค์:** เพื่อหาอุบัติการณ์ของเชื้อแบคทีเรียก่อโรคในทวารหนักที่ดื้อต่อยากลุ่ม *fluoroquinolone* และศึกษาถึงประสิทธิภาพของการทำความสะอาดทวารหนักด้วยน้ำยาฆ่าเชื้อ ก่อนเจาะตรวจชิ้นเนื้อต่อมลูกหมาก

**วัสดุและวิธีการ:** อาสาสมัคร 105 ราย ที่มีค่า PSA มากกว่า 4 ng/ml หรือ คล่าต่อมลูกหมากมีลักษณะผิดปกติ ที่ต้องเจาะชิ้นเนื้อต่อมลูกหมาก เข้าร่วมการศึกษาระหว่างเดือนธันวาคม พ.ศ. 2555 ถึง มีนาคม พ.ศ. 2556 ก่อนเจาะเนื้อต่อมลูกหมาก อาสาสมัครแต่ละรายจะได้รับการตรวจเพาะเชื้อจากทวารหนัก 2 ครั้ง คือก่อนและหลังสวนล้างทวารหนักด้วยน้ำยาฆ่าเชื้อเบตาดีน จากนั้นเปรียบเทียบปริมาณและชนิดของเชื้อที่ได้ และเฝ้าบันทึกติดตามการติดเชื้อหลังการเจาะชิ้นเนื้อต่อมลูกหมากภายใน 30 วัน

**ผลการศึกษา:** ก่อนสวนล้างพบเชื้อแบคทีเรียในทวารหนักของอาสาสมัคร 90 ราย ไม่พบเชื้อ 15 ราย หลังสวนล้างเหลือพบเชื้อแบคทีเรียในทวารหนักเพียง 53 ราย ( $p < 0.001$ ) อีก 37 ราย เชื้อลดลงจนไม่พบเชื้ออีก ส่วนในในบรรดา 53 ราย ที่ยังพบเชื้อหลังสวนล้างทวารหนัก แบ่งเป็น 36 ราย เชื้อเท่าเดิม 4 ราย มีเชื้อเพิ่มขึ้น 13 ราย เชื้อลดลง และพบว่ามี 81 ใน 90 ราย (90%) ที่มีเชื้อในทวารหนักที่ดื้อต่อยากลุ่ม *fluoroquinolone* ซึ่งส่วนใหญ่เป็นเชื้อ *E. coli*

**สรุป:** อุบัติการณ์ของเชื้อก่อโรคในทวารหนักที่ดื้อต่อยากลุ่ม *fluoroquinolone* ในโรงพยาบาลรามธิบดี คิดเป็นประมาณ 90% โดยพบเชื้อ *E. coli* ได้บ่อยที่สุด และการสวนล้างทวารหนักก่อนเจาะเนื้อต่อมลูกหมาก สามารถลดอุบัติการณ์โดยรวมของการเพาะเชื้อพบแบคทีเรียได้อย่างมีนัยสำคัญ

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