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Brief Original Article

Risk factors for infection development after transrectal prostate biopsy and the role of resistant bacteria in colonic flora

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Abstract

Introduction: In this study, we aimed to identify risk factors for the development of infectious complications after prostate biopsy and to investigate the role of intestinal colonization of bacteria that are resistant to prophylactic antibiotics.

Methodology: A total of 168 patients who had undergone transrectal prostate biopsy (TRPB) under ciprofloxacin and gentamycin prophylaxis were included in the study. Stool cultures and subsequent antibiotic susceptibility testing were performed in all patients before the start of antibiotic prophylaxis.

Results: Of the 168 patients, 17 (10.1%) developed urinary tract infection (UTI), while 6 (3.57%) developed sepsis within seven days after biopsy. Ciprofloxacin-resistant bacterial colonization was detected in 81 (48.2%) of the patients. None of the patients with ciprofloxacin-sensitive bacteria in intestinal flora developed a UTI. The colonization of intestinal ciprofloxacin-resistant bacteria increased UTI risk significantly after TRPB ($p < 0.0001$). Urolithiasis history, presence of permanent urinary catheterization, hospitalization history for more than 48 hours in the last year, and recent antibiotic usage significantly increased UTI risk after TRPB.

Conclusions: Development of an infection was more frequent in patients with resistant bacterial colonization. We hope to guide more comprehensive studies designed to find a standard prophylactic regimen for TRPB that can be used all over the world.

Key words: Prostate biopsy; urinary tract infection; intestinal flora; quinolone resistance; prophylaxis.

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Introduction

Transrectal prostate biopsy (TRPB) is the standard procedure in the diagnosis of prostate cancer [1,2]. Even though it is well tolerated, it is not totally risk-free, as is the case in any other invasive procedures [3]. After bleeding complications, urinary tract infection (UTI) is the second-most frequently noted complication of TRPB [4].

Many reports indicate that antibiotic prophylaxis decreases the incidence of symptomatic infections, but the optimal prophylactic regimen has not yet been established [5]. Fluoroquinolones provide a broad-spectrum coverage for *Escherichia coli*, which is the most common etiologic agent in infections after prostate biopsy [6].

The aim of this study was to define risk factors for UTI development after prostate biopsy. Furthermore, considering resistance status of colonic bacteria, our aim was to determine the most appropriate antibiotic that could be used for TRPB prophylaxis.

Methodology

A total of 168 patients who had undergone TRPB between July 2010 and February 2011 were enrolled in

Table 1. Antibiotic sensitivity results of ciprofloxacin-resistant *E. coli* isolates (n = 74).

	Sensitive	Intermediate	Resistant
Levofloxacin	6 (8.1%)	16 (21.6%)	52 (70.3%)
Gentamicin	42 (56.8%)	0	32 (43.2%)
Amikacin	74 (100%)	0	0
Nitrofurantoin	72 (97.3%)	1 (1.4%)	1 (1.4%)
Fosfomycin	73 (98.6%)	0	1 (1.4%)
Cefotaxim	46 (62.2%)	3 (4.1%)	25 (33.8%)
Ceftazidime	57 (77.0%)	4 (5.4%)	13 (17.6%)
Trimethoprim-sulfamethoxazole	22 (29.7%)	0	52 (70.3%)
Amoxicillin-clavulanate	23 (31.1%)	9 (12.2%)	42 (56.8%)
Ertapenem	72 (97.3%)	0	2 (2.7%)

the study prospectively. Ethical approval was received from the ethics committee of Ankara University. The relationship between UTI and age, presence of chronic renal disease, presence of diabetes, malignancy history, usage of immunosuppressive drugs, history of urological surgery, urolithiasis, permanent urinary catheterization, history of hospitalization > 48 hours, UTI history, recent antibiotic usage, and biopsy result as benign or malignant were assessed.

All of the patients received 500 mg oral ciprofloxacin every 12 hours for 5 days, starting 12 hours before biopsy, and 80 mg intramuscular gentamicin starting 1–2 hours before biopsy, every 12 hours, for a total of three doses. Patients with dysuria and pyuria in urinalysis within 7 days after biopsy were considered as having a UTI related to TRPB. Sepsis was diagnosed if at least two of the systemic inflammatory response syndrome criteria were positive with an accompanying positive culture [7].

Stool samples were taken 1–15 days before the start of prophylaxis. Ciprofloxacin minimum inhibitory concentration (MIC) value for *Enterobacteriaceae* was ≥ 4 mg/L for resistance. Thus, stool samples were inoculated onto eosine methylene blue (EMB) agar (Levine, BD, Le Pont de Claix, France) comprising 4 mg/L ciprofloxacin. Extended-spectrum beta lactamase (ESBL) presence was investigated with cefotaxime/cefotaxime-clavulanate, ceftazidime/ceftazidime-clavulanate disks (Becton Dickinson, Sparks, USA).

Statistical analysis was performed using Fisher's exact test and logistic regression analysis. Comparisons were performed using SPSS version 15.0 statistical program, and the level of significance was set at $p < 0.005$.

Results

Of the 168 patients, 17 (10.1%) developed a UTI, and 6 (3.57%) developed sepsis within seven days after biopsy. The mean age of the patients was 63.31 ± 7.86 years (range, 44–84). Ciprofloxacin-resistant bacterial colonization was detected in 81 (48.2%) of the patients. Of these 81 resistant bacteria, 74 (91.3%) were *E. coli*, 5 (6.2%) were *Enterococcus* spp., and 2 (2.5%) were *Klebsiella* spp. Twenty-nine *E. coli* and one *Klebsiella* spp. isolates were ESBL positive. Antibiotic sensitivity results of ciprofloxacin-resistant *E. coli* isolates is shown in Table 1. None of the patients with ciprofloxacin-sensitive bacteria in intestinal flora developed a UTI. All the patients who developed a UTI

Table 2. Risk factors for infectious complications.

Variable	No UTİ (n = 151)	UTİ (n = 17)	Odds ratio	P value
Age > 65	63 (41.7%)	7 (41.2%)	0.978 (0.353-2.708)	1.000
Chronic renal failure	5 (3.3%)	1 (6.3%)	1.933 (0.212-17.657)	0.461
Diabetes mellitus	26 (17.3%)	2 (12.5%)	0.681 (0.146-3.180)	1.000
History of malignancy	6 (4%)	2 (12.5%)	3.452 (0.636-18.742)	0.171
History of immunosuppressive drug usage	1 (0.7%)	1 (6.3%)	10.000 (0.595-168.132)	0.183
History of urologic surgery	18 (11.9%)	3 (18.8%)	1.705 (0.443-6.567)	0.429
History of urolithiasis	24 (25.9%)	6 (37.5%)	3.175 (1.055-9.559)	0.043
Urinary catheter	2 (1.3%)	2 (12.5%)	10.643 (1.391-81.450)	0.046
History of hospitalization > 48 h	11 (7.3%)	4 (23.5%)	3.916 (1.091-14.052)	0.049
History of UTI	42 (27.8%)	7 (41.2%)	1.817 (0.649-5.085)	0.268
History of > 3 UTIs	7 (4.7%)	3 (17.6%)	4.39 (1.02-18.84)	0.03
History of antibiotic usage	74 (49%)	14 (82.4%)	4.856 (1.341-17.590)	0.019
Prostate malignancy	54 (35.8%)	8 (47.1%)	1.597 (0.582-4.379)	0.516

were colonized by ciprofloxacin-resistant pathogens. Colonization of intestinal ciprofloxacin-resistant bacteria increased UTI risk significantly after TRPB ($p < 0.0001$).

Of the 168 patients, 88 (52.4%) had used antibiotics for more than 48 hours in the last 3 months before the biopsy. Sixty-six of them (75%) had a history of using fluoroquinolones. In the univariate analysis, age over 65 years, presence of chronic renal disease, presence of diabetes, malignancy history, use of immune suppressive drugs, history of urological surgery, and detection of malignancy in prostate biopsy specimen were statistically insignificant risk factors (Table 2). Urolithiasis history, presence of permanent urinary catheterization, hospitalization history for more than 48 hours in the last year, and recent antibiotic usage increased UTI risk significantly after TRPB (Table 2). The risk factors according to the microorganisms can be seen in table 3.

Discussion

Infectious complications after TRPB are not uncommon, but antibiotic prophylaxis has significantly decreased their incidence [2,4]; however, an appropriate prophylactic antibiotic regimen has not been established. Fluoroquinolones have been extensively studied in the prophylaxis of TRPB. In our study, ciprofloxacin and gentamycin combination was the prophylactic regimen.

Simple UTIs frequently occur after biopsy (1.2%–11.3 %), and UTIs with fever are also common (1.4%–4.5 %) [2,4,8]. Sepsis is the most serious complication of prostate biopsy and is encountered in 0.1%–2.7 % of patients [2,5,9]. The results of our study were similar to those found in the literature.

Several recent studies identify both patient and procedural risk factors for infectious complications [10,11]. Patient-specific risk factors identified include underlying medical comorbidities (particularly diabetes mellitus) and recent hospitalization [10,12]. In our study, comorbidities such as chronic renal failure and diabetes mellitus were insignificant risk factors (Table 2). Hospitalization of more than 48 hours' duration in the preceding year was noted as a risk factor in our study. In a recent study, patients who had been hospitalized in the month preceding TRPB were significantly more likely to develop urosepsis than those without a history of hospitalization (odds ratio: 8.63; 95% confidence interval: 1.48–50.4; P = .02) [14]. History of more than three occurrences of UTI and history of antibiotic usage in the preceding three months were found to be significant risk factors for infection after TRPB in our study.

Pre-existing urological pathology may also increase the risk of infectious complications. Presence of a urinary catheter was found to be a significant risk factor for UTIs in our study. One study noted that long-term urethral catheterization increases UTI risk compared to patients without catheters (19.2% vs. 3.06%; $p < 0.0001$) [2]. Another pre-existing urological pathology that was a significant risk factor for infection in our study was the presence of urolithiasis history.

In recent years, many researchers have been investigating the role of gastrointestinal resistant bacterial colonization in resistant bacterial infections [13]. It is well known that commensal flora is a natural reservoir for the development of bacterial infections [14]. During TRPB, inoculation of bacterial flora into prostate tissue, blood vessels, or urine is important for infectious complications. Colonization of intestinal flora with resistant bacteria is even more important for this patient group in particular.

Batura *et al.* found that the ratio of carrying ciprofloxacin-resistant bacteria in intestinal flora was

Table 3. Risk factors according to microorganism.

Variable	*E. coli*	*Enterococcus*	*Klebsiella*
Age > 65	34 (45.9%)	-	1 (50.0%)
Chronic renal failure	2 (2.7%)	1 (20.0%)	-
Diabetes mellitus	14 (18.9%)	-	-
History of malignancy	3 (4.0%)	1 (20.0%)	-
History of immunosuppressive drug usage	2 (2.7%)	-	-
History of urologic surgery	9 (12.2%)	2 (40.0%)	-
History of urolithiasis	15 (20.3%)	1 (20.0%)	-
Urinary catheter	4 (5.4%)	-	-
History of hospitalization > 48 h	9 (12.2%)	-	-
History of UTI	34 (45.9%)	-	-
History of > 3 UTIs	7 (9.5%)	-	-
History of antibiotic usage	57 (77.0%)	2 (40%)	-
Prostate malignancy	24 (32.4%)	2 (40%)	2 (100%)

11%, and 1/6 of these patients developed ciprofloxacin-resistant infections after TRPB [15]. In our study, the ratio of carrying ciprofloxacin-resistant bacteria in intestinal flora was 48.2%, and 1/5 of patients carrying ciprofloxacin-resistant bacteria in intestinal flora developed infections after TRPB. No infection related to TRPB developed in the patients with ciprofloxacin-sensitive bacterial colonization. We therefore concluded that colonization of intestinal fluoroquinolone-resistant bacteria increased infection risk after TRPB. In our study, nearly half of the patients were colonized with resistant bacteria. The reason for this can be a history of long-term antibiotic use in a significant number of patients. In this study, we found ESBL-positive *Enterobacteriaceae* colonization in 1/6 of our patients. It should be kept in mind that when only ciprofloxacin-resistant *Enterobacteriaceae* are isolated using selective media, the real ESBL-positive bacteria ratio can be higher.

The most frequently isolated infectious pathogen after TRPB is *E. coli* [3,5]. For this reason, it is important to know sensitivity of fecal *E. coli* isolates when choosing the prophylactic agent. There are some limitations to our study. One is the small sample size. Our study was not designed to determine the appropriate prophylactic regimen.

Conclusions

In this study, development of infection was more frequent in patients with resistant bacterial colonization. We hope to guide more comprehensive studies designed to find a standard prophylactic regimen for TRPB that can be used all over the world.

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References

1. Djavan B, Margreiter M (2007) Biopsy standards for detection of prostate cancer. World J Urol 25: 11-17.
2. Simsir A, Kismali E, Mammadov R, Gunaydın G, Cal C (2010) Is it possible to predict sepsis, the most serious complication in prostate biopsy? Urol Int 84: 395-399.
3. Lee SH, Chen SM, Ho CR, Chang PL, Chen CL, Tsui KL (2009) Risk factors associated with transrectal ultrasound guided prostate needle biopsy in patients with prostate cancer. Chang Gung Med J 32: 623-627.
4. Zaytoun OM, Vargo EH, Rajan R, Berglund R, Gordon S, Jones JS (2011) Emergence of fluoroquinolone-resistant *Escherichia coli* as cause of post prostate biopsy infection: implications for prophylaxis and treatment. Urology 77: 1035-1041.
5. Shandera KC, Thibault GP, Deshon GE (1998) Variability in patient preparation for prostate biopsy among American urologists. Urology 52: 644-646.
6. Naber KG (1989) Use of quinolones in urinary tract infections and prostatitis. Rev Infect Dis 11: 1321-1327.
7. Sobel JD, Kaye D (2005) Urinary tract infections. In Mandell GL, Bennet JE, Dolin R, editors. Principles and practice of infectious diseases. Philadelphia: Chuchill Livingstone. 957-987.
8. Otrock ZK, Oghlakian GO, Salamoun MM, Haddad M, Bizri AR (2004) Incidence of urinary tract infection following transrectal ultrasound guided prostate biopsy at a tertiary-care medical center in Lebanon. Infect Control Hosp Epidemiol 25: 873-877.
9. Hadway P, Barrett LK, Waghorn DJ, Hasan K, Bdesha A, Haldar N, Kelleher J (2009) Urosepsis and bacteraemia caused by antibiotic-resistant organisms after transrectal ultrasonography-guided prostate biopsy. BJU Int 104: 1556-1558.
10. Loeb S, Carter HB, Berndt SI, Ricker W, Schaeffer EM (2011) Complications after prostate biopsy: data from SEER-Medicare. J Urol 186: 1830-1834.
11. Loeb S, van den Heuvel S, Zhu X, Bangma CH, Schröder FH, Roobol MJ (2012) Infectious complications and hospital admissions after prostate biopsy in a European randomized trial. Eur Urol 61: 1110-1114.
12. Carignan A, Roussy JF, Lapointe V, Valiquette L, Sabbagh R, Pépin J (2012) Increasing risk of infectious complications after transrectal ultrasoundguided prostate biopsies: time to reassess antimicrobial prophylaxis? Eur Urol 62: 453-459.
13. Lautenbach E, Santana E, Lee A, Tolomeo P, Black N, Babson A, Perencevich EN, Harris AD, Smith CA, Maslow J (2008) Efficient recovery of fluoroquinolone-susceptible and fluoroquinolone-resistant *Escherichia coli* strains from frozen samples. Infect Control Hosp Epidemiol 29: 367-369.
14. de Lastours V, Chau F, Tubach F, Pasquet B, Ruppé E, Fantin B (2010) Independent behavior of commensal flora for carriage of fluoroquinolone-resistant bacteria in patients at admission. Antimicrob Agents Chemother 54: 5193-5200.
15. Batura D, Rao GG, Nielsen PB (2010) Prevalence of antimicrobial resistance in intestinal flora of patients undergoing prostatic biopsy: implications for prophylaxis and treatment of infections after biopsy. BJU Int 106: 1017-1020.

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