

Infection/Inflammation

Risk Factors for Acute Prostatitis after Transrectal Biopsy of the Prostate

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Purpose: To investigate the incidence, clinical features, pathogenic bacteria, and risk factors associated with acute prostatitis after transrectal prostate biopsy.

Materials and Methods: We retrospectively reviewed the medical records of 923 transrectal ultrasound-guided needle biopsies of the prostate in 878 patients performed at our institution from June 2004 to May 2009. The indications for biopsy were generally serum prostate-specific antigen (PSA) elevation, abnormal findings on a digital rectal examination, or both. All biopsies were performed with the patient hospitalized except for 10 patients who refused to be hospitalized, and ciprofloxacin was administered as an antibiotic prophylaxis. The incidence, clinical features, pathogenic bacteria, and potential risk factors associated with acute prostatitis after prostate biopsy were evaluated.

Results: Acute prostatitis developed in 18 (2.0%) cases after prostate biopsy. Among them, 9 (1.0%) had bacteremia and 2 (0.2%) showed clinical features of sepsis. Of the total 50 urine or blood specimens sent for culture study, 27 (54.0%) specimens showed positive cultures, including *E. coli* in 25. Among the 27 culture-positive specimens, 26 (96.3%) were resistant to ciprofloxacin. Among the potential risk factors for acute prostatitis after prostate biopsy, biopsy performed as an outpatient procedure without a cleansing enema ($p=0.001$) and past history of cerebrovascular accident ($p=0.048$) were statistically significant.

Conclusions: Fluoroquinolone is effective as an antibiotic prophylaxis for transrectal prostate biopsy in most cases. The incidence of acute prostatitis after transrectal prostate biopsy was 2.0%, and almost all cases were caused by fluoroquinolone-resistant *E. coli*. A cleansing enema is recommended before transrectal prostate biopsy.

Key Words: Biopsy; Prostate; Prostatitis

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INTRODUCTION

Transrectal ultrasound-guided needle biopsy of the prostate is generally accepted as the standard diagnostic procedure for detecting prostate cancer [1-4]. Although transrectal ultrasound-guided prostate biopsy is generally considered to be a safe procedure, complications are occasionally encountered. These include minor complications such as hematuria, hemospermia, and rectal bleeding as well as clinically significant, major complications such as acute prostatitis and urosepsis, which may be fatal [5-8].

Antibiotic prophylaxis before transrectal prostate biopsy

is generally accepted to reduce the infection-related complications. Fluoroquinolones, which are known to be delivered at high concentrations in the prostate, are considered to be effective in lowering the incidence of infective complications [9-12]. However, there are recent reports of the development of fluoroquinolone-resistant infections after transrectal prostate biopsy [13-16].

The number of prostate biopsies is bound to progressively increase with the advent of prostate-specific antigen (PSA) screening and increasing awareness of prostate cancer. Therefore, it becomes essential to have a clear understanding of the morbidity of transrectal prostate biopsy

opsy to allow for more appropriate patient counseling and management.

In this study, we investigated the incidence, clinical features, pathogenic bacteria, and risk factors associated with acute prostatitis after transrectal prostate biopsy.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 923 prostate biopsies, including 77 repeated biopsies, performed in 878 patients at our institution from June 2004 to May 2009. The indications for prostate biopsy were serum PSA elevation or abnormal findings on a digital rectal examination or transrectal ultrasonography. All prostate biopsies were performed transrectally under ultrasound guidance by a radiologist. An automatic biopsy gun with an 18-gauge needle was used to obtain the biopsy specimens. Either 10- or 12-core biopsies were sampled depending on the time period during which the biopsy was performed. Ten-core biopsies were performed from June 2004 to April 2008, and 12-core biopsies were performed since May 2008. As a rule, acetylsalicylic acid or oral anticoagulant agents were stopped 7 days before prostate biopsy with the approval of the prescribing physician. Urine samples were obtained for urinalysis before prostate biopsy in all cases except 5 and for urine culture in all cases except 10.

All prostate biopsies were performed with the patient hospitalized except for 10 patients who refused to be hospitalized. In patients who were hospitalized, 200 mg ciprofloxacin was injected intravenously before and after the biopsy. All hospitalized patients received a cleansing enema before biopsy. They were discharged from the hospital on the following morning after the biopsy and received 250 mg ciprofloxacin orally twice daily for 7 days. Patients who underwent the biopsy on an outpatient basis did not receive a cleansing enema or parenteral injections of ciprofloxacin. These patients received 250 mg ciprofloxacin orally twice daily for 7 days, beginning on the morning before biopsy. If symptoms of acute prostatitis, such as fever, chills, and voiding difficulty, developed after prostate biopsy, the patient was readmitted for treatment including intravenous antibiotics.

The incidence, clinical features, and pathogenic bacteria of acute prostatitis after prostate biopsy were investigated. Variables such as the patient's age, past medical history, prostate volume, biopsy core numbers, number of biopsy sessions, cleansing enema, and urinalysis and urine culture findings before biopsy were also assessed.

Statistical analysis was performed by using the chi-square test or independent t-test with SPSS version 13.0 (SPSS Inc., Chicago, USA). Values of $p < 0.05$ were considered to be statistically significant in all of the analyses.

RESULTS

Of the 923 prostate biopsy cases, acute prostatitis developed in 18 (2.0%) cases after prostate biopsy. Among these

18 cases, 9 (1.0%) had bacteremia as confirmed by positive blood culture, and 2 (0.2%) showed clinical features of sepsis. The patients developed infective symptoms a median of 1 day (mean, 2.8 days; range, 1-25 days) after prostate biopsy.

Of the 18 cases with acute prostatitis, 13 (72.2%) cases had positive urine and/or blood cultures, including *E. coli* in 11, *Klebsiella pneumoniae* in 1, and *Citrobacter freundii* in 1. Of the total 50 urine or blood specimens sent for culture study, 27 (54.0%) specimens showed positive cultures, including *E. coli* in 25, *Klebsiella pneumoniae* in 1, and *Citrobacter freundii* in 1. Among the 27 culture-positive specimens, 26 (96.3%) yielded ciprofloxacin-resistant pathogens, including *E. coli* in 24, *Klebsiella pneumoniae* in 1, and *Citrobacter freundii* in 1. However, these pathogens were sensitive to cephalosporins and aminoglycosides (Table 1).

When stratified by year, there was no statistically significant difference in the annual rates of acute prostatitis that developed after prostate biopsy ($p=0.904$) (Table 2).

TABLE 1. Susceptibility of ciprofloxacin-resistant *E. coli* to antibiotics in 24 urine and blood culture specimens

Antibiotics	% susceptible
Trimethoprim/sulfamethoxazole	67
Ampicillin	38
Amoxicillin/clavulanic acid	86
Piperacillin	64
Piperacillin/tazobactam	100
Aztreonam	100
Imipenem	100
Tetracycline	50
Nitrofurantoin	100
Ceftazidime	100
Cefepime	100
Cefazolin	92
Cefoxitin	88
Cefotaxime	100
Ceftriaxone	100
Amikacin	100
Gentamicin	96
Netilmicin	100
Tobramycin	100

TABLE 2. Annual rates of acute prostatitis that developed after prostate biopsy

Year	No. of prostate biopsies	No. of cases with acute prostatitis (%)	p-value
2004	77	2 (2.6)	0.904
2005	124	1 (0.8)	
2006	155	4 (2.6)	
2007	218	5 (2.3)	
2008	227	4 (1.8)	
2009	122	2 (1.6)	
Total	923	18 (2.0)	

TABLE 3. Patient's age and prostate volume in relation to acute prostatitis

	Total	With acute prostatitis	Without acute prostatitis	p-value
Mean age±SD (years)	65.4±11.1	59.3±13.0	65.5±11.0	0.063
Mean prostate volume±SD (cc)	50.2±29.1	44.7±20.1	50.3±29.3	0.261

TABLE 4. Potential risk factors and rates of acute prostatitis after prostate biopsy

Risk factors	No. of prostate biopsies	No. of cases with acute prostatitis (%)	p-value
Diabetes mellitus			0.095
Yes	131	5 (3.8)	
No	792	13 (1.6)	
Hypertension			0.840
Yes	338	7 (2.1)	
No	585	11 (1.9)	
Cerebrovascular accident			0.048
Yes	54	3 (5.6)	
No	869	15 (1.7)	
Pyuria before biopsy			0.941
Yes	57	1 (1.8)	
No	861	14 (1.6)	
Urine culture before biopsy			0.771
Positive	46	1 (2.2)	
Negative	867	14 (1.6)	
No. of biopsy core			0.709
10	652	12 (1.8)	
12	271	6 (2.2)	
No. of biopsy session			0.645
1st	846	18 (2.1)	
2nd	63	0 (0)	
3rd	12	0 (0)	
4th	2	0 (0)	
Cleansing enema			0.001
Yes (biopsy in IPD)	913	15 (1.6)	
No (biopsy in OPD)	10	3 (30.0)	

IPD: inpatient department, OPD: outpatient department

The mean age of the patients who underwent prostate biopsy was 65.4 years (range, 20-95 years). The mean ages of the patients who developed acute prostatitis and of those who did not were 59.3±13.0 years and 65.5±11.0 years, respectively, which showed no statistically significant difference (p=0.063) (Table 3).

The mean prostate volume of the patients who underwent prostate biopsy was 50.2 cc (range, 12.2-383.3 cc). The mean prostate volumes of the patients who developed acute prostatitis and of those who did not were 44.7±20.1 cc and 50.3±29.3 cc, respectively, which showed no statistically significant difference (p=0.261) (Table 3).

Among the other potential risk factors for acute prostatitis after prostate biopsy, biopsy performed as an outpatient procedure without a cleansing enema (p=0.001) and past history of cerebrovascular accident (p=0.048) were statistically significant (Table 4).

DISCUSSION

Although a few studies have demonstrated that antibiotic prophylaxis may not be required for transrectal prostate biopsy [17], antibiotic prophylaxis before transrectal prostate biopsy is generally accepted to decrease the rate of infective complications [9-12]. However, there is much variability in the type, dosage, and duration of antibiotic prophylaxis [18,19].

Fluoroquinolones are the most frequently used antibiotics for prophylaxis before transrectal prostate biopsy because of their broad spectrum of action, which is adequate for common urinary and colorectal flora; their high concentration within the prostatic tissue; and the ease of oral administration [20]. Numerous studies have demonstrated a decrease in infective complications with fluoroquinolone use to rates of less than 1% to 4% [9,10,12-14, 21]. In our study, the rate of acute prostatitis was 2.0%, which is consistent with the previously reported rates. This means that fluoroquinolone is effective as an antibiotic prophylaxis for transrectal prostate biopsy in most cases.

However, recent reports have shown that fluoroquinolone-resistant infections following transrectal prostate biopsy are emerging [9,10,13-16,21]. Shigehara et al reported that all of the urine cultures of patients with acute prostatitis that developed after transrectal prostate biopsy yielded levofloxacin-resistant *E. coli* [9]. Feliciano et al showed that 61% of the patients with infective complications after transrectal prostate biopsy had positive urine and/or blood cultures. Of the positive cultures, those from 89% of patients yielded *E. coli* and 90% were fluoroquinolone-resistant. The incidence of infective complications and fluoroquinolone-resistant infections in 2006 were 3 times and 3.3 to 4.3 times higher than in 2004 and 2005, respectively [13]. Özden et al reported that 61% of the patients with acute prostatitis after transrectal prostate biopsy had positive cultures, with *E. coli* being the most common pathogen (82%). Among the patients infected with *E. coli*, 93% showed fluoroquinolone resistance and 43% harbored extended-spectrum β -lactamase-producing *E. coli* [16]. In our study, 72.2% of cases with acute prostatitis after transrectal prostate biopsy had positive urine and/or blood cultures. Of the positive cultures, 96.3% were resistant to ciprofloxacin. However, in contradiction to the findings by Feliciano et al, there was no significant difference in the annual rates of acute prostatitis after prostate biopsy [13].

Özden et al suggested that the increasing fluoroquinolone resistance might be due to the previous wide use of these drugs [16]. Shigehara et al considered that the previous use of levofloxacin might cause bacterial selection in the rec-

tum, and levofloxacin-resistant *E. coli* might then appear in the rectum for a certain period [9]. In their reports, acute prostatitis developed more frequently after repeat biopsy than after the first biopsy [9,16]. However, in our study, the rate of acute prostatitis did not differ according to the number of biopsy sessions, and all cases of acute prostatitis occurred after the first biopsy.

Because our results showed that ciprofloxacin-resistant pathogens were sensitive to cephalosporins and aminoglycosides, empirical treatment with cephalosporins or aminoglycosides is recommended in patients with acute prostatitis that develops after transrectal prostate biopsy until culture-specific therapy can be implemented.

The impact of cleansing enemas before transrectal prostate biopsy on the infective complications is still controversial. Whereas some studies have shown that a cleansing enema is not required or recommended before biopsy [22,23], others have suggested that a cleansing enema before biopsy may decrease bacteremia and bacteriuria after prostate biopsy [24,25]. A cleansing enema has the advantage of producing a superior acoustic window for prostate imaging by decreasing the amount of feces in the rectum. Furthermore, a cleansing enema and an empty rectal vault may reduce bacterial seeding of the prostate [26].

In our series of 923 prostate biopsy cases, all patients except 10 (1.1%) received a cleansing enema. Acute prostatitis developed more frequently in cases without a cleansing enema than in those with a cleansing enema before biopsy, and this difference was statistically significant. Because only 1.1% of our cases did not receive a cleansing enema, however, a large, prospective randomized study will be needed to clarify the impact of a cleansing enema on infective complications.

In our study, biopsy performed as an outpatient procedure without a cleansing enema and past history of cerebrovascular accident were statistically significant risk factors for acute prostatitis after transrectal prostate biopsy. Pyuria and positive urine culture before biopsy were not significant risk factors, which is consistent with the findings of Ecke et al that positive microbiology in urine before prostate biopsy is not a risk factor for a higher infection rate [27]. Chiang et al suggested that patients with a larger prostate (> 45 ml) had a significantly higher risk of developing acute prostatitis and acute urinary retention after prostate biopsy than did those with a smaller prostate (< 45 ml) [28]. However, in our study, prostate volume was not a significant risk factor for acute prostatitis after prostate biopsy.

In our study, patient's age, diabetes mellitus, hypertension, and number of biopsy cores were not significant risk factors for acute prostatitis after prostate biopsy, which is consistent with the results of a study by Chiang et al [28]. Past history of cerebrovascular accident was a statistically significant risk factor for acute prostatitis after prostate biopsy in our study, but not in the report by Chiang et al [28]. The possible explanation is that the patients with a history of cerebrovascular accident may have

altered bowel function and constipation [29,30], which may result in a change in the bacterial flora in the rectum. They also could have consumed fluoroquinolones before prostate biopsy. These combined might lead to the appearance of fluoroquinolone-resistant pathogens in the rectum and an increase in infective complications after transrectal prostate biopsy.

A limitation of our study is that it was retrospective in nature, and the sample size of the groups was limited because of the low incidence of acute prostatitis after transrectal prostate biopsy. All patients except 10 (1.1%) were hospitalized and received a cleansing enema before transrectal prostate biopsy. Further prospective studies will be necessary to confirm the impact on infective complications of a cleansing enema before transrectal prostate biopsy.

CONCLUSIONS

Fluoroquinolone is effective as an antibiotic prophylaxis for transrectal prostate biopsy in most cases. The incidence of acute prostatitis after transrectal prostate biopsy was 2.0%, and almost all cases were caused by fluoroquinolone-resistant *E. coli*. A cleansing enema is recommended before transrectal prostate biopsy. Empirical treatment with cephalosporins or aminoglycosides should be initiated for patients with acute prostatitis after transrectal prostate biopsy until culture-specific therapy can be implemented.

Conflicts of Interest

The authors have nothing to disclose.

REFERENCES

1. de la Rosette JJ, Wink MH, Mamoulakis C, Wondergem N, ten Kate FJ, Zwinderman K, et al. Optimizing prostate cancer detection: 8 versus 12-core biopsy protocol. *J Urol* 2009;182:1329-36.
2. Lee SE. Diagnosis of prostate cancer. *Korean J Urol* 2004;45:197-208.
3. Chae Y, Kim YJ, Kim T, Yun SJ, Lee SC, Kim WJ. The comparison between transperineal and transrectal ultrasound-guided prostate needle biopsy. *Korean J Urol* 2009;50:119-24.
4. Jeon SB, Zhao C, Jung YB, Park YK, Park JK. A protocol for transrectal, ultrasonography-guided, 41-core prostate needle biopsy. *Korean J Urol* 2008;49:122-6.
5. Berger AP, Gozzi C, Steiner H, Frauscher F, Varkarakis J, Rogatsch H, et al. Complication rate of transrectal ultrasound guided prostate biopsy: a comparison among 3 protocols with 6, 10 and 15 cores. *J Urol* 2004;171:1478-80.
6. Djavan B, Waldert M, Zlotta A, Dobronski P, Seitz C, Remzi M, et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. *J Urol* 2001;166:856-60.
7. Raaijmakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schröder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. *Urology* 2002;60:826-30.
8. Nam RK, Saskin R, Lee Y, Liu Y, Law C, Klotz LH, et al. Increasing

- hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. *J Urol* 2010;183:963-8.
9. Shigehara K, Miyagi T, Nakashima T, Shimamura M. Acute bacterial prostatitis after transrectal prostate needle biopsy: clinical analysis. *J Infect Chemother* 2008;14:40-3.
 10. Yamamoto S, Ishitoya S, Segawa T, Kamoto T, Okumura K, Ogawa O. Antibiotic prophylaxis for transrectal prostate biopsy: a prospective randomized study of tosufloxacin versus levofloxacin. *Int J Urol* 2008;15:604-6.
 11. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. *BJU Int* 2000;85:682-5.
 12. Sieber PR, Rommel FM, Agusta VE, Breslin JA, Huffnagle HW, Harpster LE. Antibiotic prophylaxis in ultrasound guided transrectal prostate biopsy. *J Urol* 1997;157:2199-200.
 13. Feliciano J, Teper E, Ferrandino M, Macchia RJ, Blank W, Grunberger I, et al. The incidence of fluoroquinolone resistant infections after prostate biopsy--are fluoroquinolones still effective prophylaxis? *J Urol* 2008;179:952-5.
 14. Sieber PR, Rommel FM, Theodoran CG, Hong RD, Del Terzo MA. Contemporary prostate biopsy complication rates in community-based urology practice. *Urology* 2007;70:498-500.
 15. Tal R, Livne PM, Lask DM, Baniel J. Empirical management of urinary tract infections complicating transrectal ultrasound guided prostate biopsy. *J Urol* 2003;169:1762-5.
 16. Özden E, Bostanci Y, Yakupoglu KY, Akdeniz E, Yilmaz AF, Tulek N, et al. Incidence of acute prostatitis caused by extended-spectrum beta-lactamase-producing *Escherichia coli* after transrectal prostate biopsy. *Urology* 2009;74:119-23.
 17. Enlund AL, Varenhorst E. Morbidity of ultrasound-guided transrectal core biopsy of the prostate without prophylactic antibiotic therapy. A prospective study in 415 cases. *Br J Urol* 1997;79:777-80.
 18. Shandera KC, Thibault GP, Deshon GE Jr. Variability in patient preparation for prostate biopsy among American urologists. *Urology* 1998;52:644-6.
 19. Lee G, Attar K, Laniado M, Karim O. Trans-rectal ultrasound guided biopsy of the prostate: nationwide diversity in practice and training in the United Kingdom. *Int Urol Nephrol* 2007;39:185-8.
 20. Cormio L, Berardi B, Callea A, Fiorentino N, Sblendorio D, Zizzi V, et al. Antimicrobial prophylaxis for transrectal prostatic biopsy: a prospective study of ciprofloxacin vs piperacillin/tazobactam. *BJU Int* 2002;90:700-2.
 21. Jang HA, Kang JI, Bae YD, Jin MH, Park JY, Moon DG, et al. Risk factors of the infectious complications and causative microorganisms after transrectal ultrasound-guided prostate needle biopsy. *Korean J Androl* 2008;26:212-7.
 22. Carey JM, Korman HJ. Transrectal ultrasound guided biopsy of the prostate. Do enemas decrease clinically significant complications? *J Urol* 2001;166:82-5.
 23. Kang MY, Park JH, Kwak C, Paick JS, Kim HH. Transrectal needle biopsy of the prostate: the efficacy of a pre-biopsy enema. *Korean J Urol* 2008;49:248-51.
 24. Lindert KA, Kabalin JN, Terris MK. Bacteremia and bacteriuria after transrectal ultrasound guided prostate biopsy. *J Urol* 2000;164:76-80.
 25. Brown RW, Warner JJ, Turner BI, Harris LF, Alford RH. Bacteremia and bacteriuria after transrectal prostatic biopsy. *Urology* 1981;18:145-8.
 26. Ramey JR, Halpern EJ, Gomella LG. Ultrasonography and biopsy of the prostate. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. *Campbell-Walsh urology*. 9th ed. Philadelphia: Saunders; 2007;2883-95.
 27. Ecke TH, Gunia S, Bartel P, Hallmann S, Koch S, Ruttloff J. Complications and risk factors of transrectal ultrasound guided needle biopsies of the prostate evaluated by questionnaire. *Urol Oncol* 2008;26:474-8.
 28. Chiang IN, Chang SJ, Pu YS, Huang KH, Yu HJ, Huang CY. Major complications and associated risk factors of transrectal ultrasound guided prostate needle biopsy: a retrospective study of 1875 cases in Taiwan. *J Formos Med Assoc* 2007;106:929-34.
 29. Krogh K, Christensen P, Laurberg S. Colorectal symptoms in patients with neurological diseases. *Acta Neurol Scand* 2001;103:335-43.
 30. Bracci F, Badiali D, Pezzotti P, Scivoletto G, Fuoco U, Di Lucente L, et al. Chronic constipation in hemiplegic patients. *World J Gastroenterol* 2007;13:3967-72.